STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 193511

TO: David Lukton
Location: REM/3B75/3C18
Art Unit: 1654
June 23, 2006

Case Serial Number: 10/775598

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

ACCESS DB # 193511

PLEASE PRINT CLEARLY

SEARCH REQUEST FORM
(STIC)

Requestor's Name: David Lukton Examiner number: 71263 Date: 6/21/06

Art Unit: 1654 Phone number: 571-272-0952 Serial Number: 10-775 598

Mail Box: 3-C-18 Examiner Rm: 3-B-75 Results format: paper

* * * * * * * *

Title: INHIBITORS OF DIPEPTIDYL-AMINOPEPTIDASE TYPE IV

Applicants: BACHOVCHIN, WILLIAM W.; PLAUT, ANDREW G.; FLENTKE, GEORGE R.

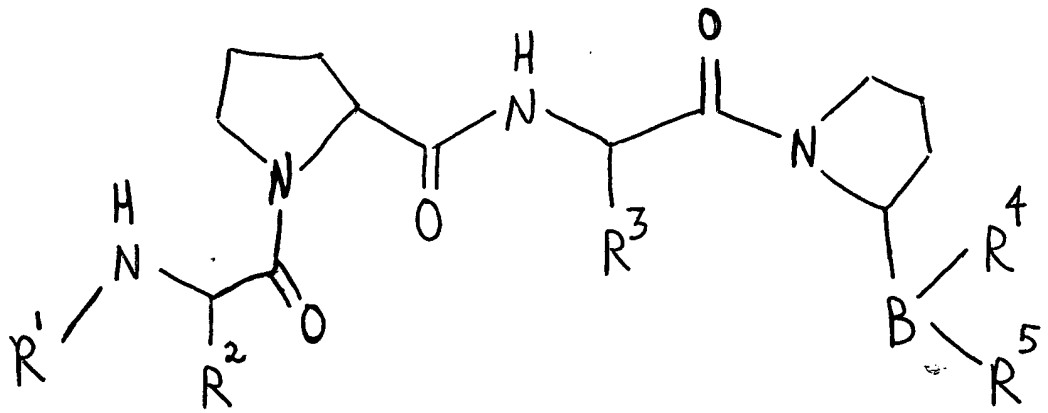
Earliest Priority Date: 10/22/91

. . . .

Applicants are claiming the compounds below.

R^1, R^2, R^3, R^4 and R^5 can be anything

"B" represents an atom of boron.



```
=> d his ful

     (FILE 'HOME' ENTERED AT 09:31:48 ON 23 JUN 2006)

     FILE 'REGISTRY' ENTERED AT 09:31:53 ON 23 JUN 2006
L7              STR
L9            304 SEA SSS FUL L7
L13             STR
L14            59 SEA SUB=L9 SSS FUL L13
L20             STR
L21             3 SEA SUB=L14 SSS FUL L20

     FILE 'HCAPLUS' ENTERED AT 09:46:35 ON 23 JUN 2006
L22             1 SEA ABB=ON  PLU=ON  L21
                D STAT QUE
                D IBIB ABS HITSTR L22 1

     FILE 'REGISTRY' ENTERED AT 09:46:55 ON 23 JUN 2006
L23            56 SEA ABB=ON  PLU=ON  L14 NOT L21

     FILE 'HCAPLUS' ENTERED AT 09:47:04 ON 23 JUN 2006
L24             2 SEA ABB=ON  PLU=ON  L23
                D STAT QUE
                D IBIB ABS HITSTR L24 1-2

     FILE 'REGISTRY' ENTERED AT 09:48:58 ON 23 JUN 2006
L25           245 SEA ABB=ON  PLU=ON  L9 NOT (L21 OR L23)

     FILE 'HCAPLUS' ENTERED AT 09:49:13 ON 23 JUN 2006
L26           234 SEA ABB=ON  PLU=ON  L25
L27           232 SEA ABB=ON  PLU=ON  L26 NOT (L22 OR L24)
L28             5 SEA ABB=ON  PLU=ON  L27 AND PD=<OCTOBER 24, 1991
                D STAT QUE L28
                D IBIB ABS HITSTR L28 1-5
L29            97 SEA ABB=ON  PLU=ON  ("BACHOVCHIN W W"/AU OR "BACHOVCHIN
                   WILLIAM"/AU OR "BACHOVCHIN WILLIAM W"/AU OR "BACHOVCHIN
                   WILLIAM WALTER"/AU)
L30            99 SEA ABB=ON  PLU=ON  "PLAUT A"/AU OR "PLAUT A G"/AU OR ("PLAUT
                   ANDREW"/AU OR "PLAUT ANDREW G"/AU)
L31            28 SEA ABB=ON  PLU=ON  ("FLENTKE G R"/AU OR "FLENTKE GEORGE"/AU
                   OR "FLENTKE GEORGE F"/AU OR "FLENTKE GEORGE R"/AU OR "FLENTKE
                   GEORGE ROBERT"/AU)
L32             1 SEA ABB=ON  PLU=ON  (L29 AND L30 AND L31) NOT (L22 OR L24 OR
                   L28)
L33             9 SEA ABB=ON  PLU=ON  L29 AND (L30 OR L31)
L34             4 SEA ABB=ON  PLU=ON  L30 AND L31
L35            21 SEA ABB=ON  PLU=ON  (L29 OR L30 OR L31) AND L27
L36            21 SEA ABB=ON  PLU=ON  (L32 OR L33 OR L34 OR L35) NOT (L22 OR L24
                   OR L28)
                D STAT QUE L36
                D IBIB ABS HITSTR L36 1-21


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   22 JUN 2006  HIGHEST RN 889059-26-1
```

DICTIONARY FILE UPDATES: 22 JUN 2006 HIGHEST RN 889059-26-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 23 Jun 2006 VOL 145 ISS 1
FILE LAST UPDATED: 22 Jun 2006 (20060622/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

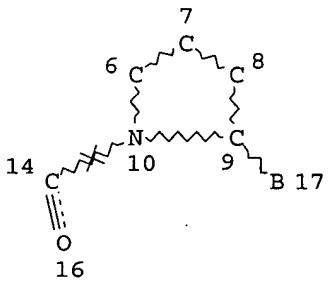
This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

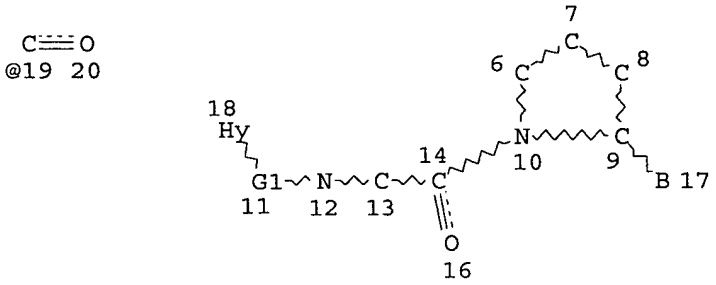
```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:46:35 ON 23 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 23 Jun 2006  VOL 145 ISS 1
FILE LAST UPDATED: 22 Jun 2006  (20060622/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L7                STR
```



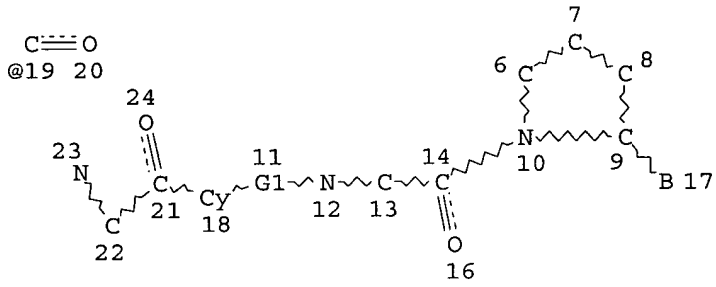

```
NODE ATTRIBUTES:
NSPEC   IS RC     AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L9           304 SEA FILE=REGISTRY SSS FUL L7
L13              STR
```



REP G1=(0-1) 19
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 18
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L14 59 SEA FILE=REGISTRY SUB=L9 SSS FUL L13
L20 STR



REP G1=(0-1) 19
NODE ATTRIBUTES:
NSPEC IS RC AT 12
NSPEC IS RC AT 13
NSPEC IS RC AT 14
NSPEC IS RC AT 21
NSPEC IS RC AT 22
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L21 3 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L22 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L21

=>
=>

```
=> d ibib abs hitstr l22 1

L22  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:892553  HCAPLUS
DOCUMENT NUMBER:          139:377254
TITLE:                    Prodrugs of Target-Activated Smart Protease Inhibitors
                          and Target-Directed Smart Protease Inhibitors
INVENTOR(S):              Bachovchin, William W.
PATENT ASSIGNEE(S):       Trustees of Tufts College, USA
SOURCE:                   PCT Int. Appl., 200 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2003092605         A2    20031113    WO 2003-US13561          20030430
     WO 2003092605         C2    20040408
     WO 2003092605         A3    20040701
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2484551            AA    20031113    CA 2003-2484551          20030430
     AU 2003228793         A1    20031117    AU 2003-228793           20030430
     EP 1499336            A2    20050126    EP 2003-726564           20030430
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2005531540         T2    20051020    JP 2004-500790           20030430
     US 2006089312         A1    20060427    US 2005-512213           20050829
PRIORITY APPLN. INFO.:                       US 2002-376636P      P   20020430
                                             WO 2003-US13561      W   20030430

OTHER SOURCE(S):          MARPAT 139:377254
```

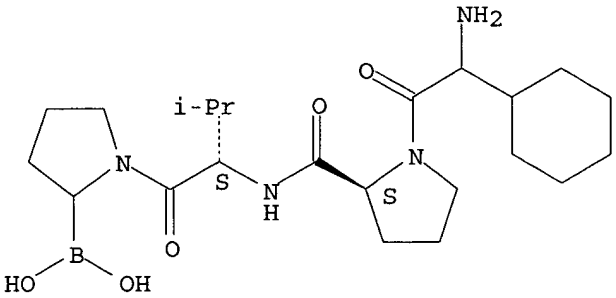
AB The present invention relates to prodrugs of protease inhibitors, such as inhibitors of proteasome, DPOP IV, FAPα and the like. These pro-inhibitors are activated, i.e., cleaved by an activated protease to release an active inhibitor moiety in proximity to a target protease: the identity of activating protease and target protease can be the same (such pro-inhibitors being referred to as Target-Activated Smart Protease Inhibitors or TASPI) or different (e.g., Target-Directed Smart Protease Inhibitors or TDSPI). After activation of the pro-inhibitor, the active inhibitor moiety can self-inactive by, e.g., intramol.-cyclization or cis-trans isomerization.

IT **623148-92-5 623148-93-6**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DPP IV-activated DPP IV inhibitor; prodrugs of TASPI (Target-Activated Smart Protease Inhibitors) and TDSPI (Target-Directed Smart Protease Inhibitors))

RN 623148-92-5 HCAPLUS
CN L-Prolinamide, 2-cyclohexylglycyl-N-[(1S)-1-[(2-borono-1-

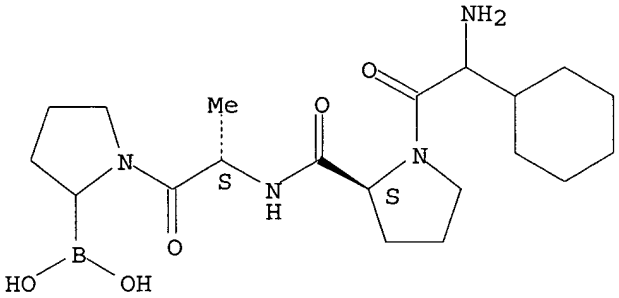
pyrrolidinyl)carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



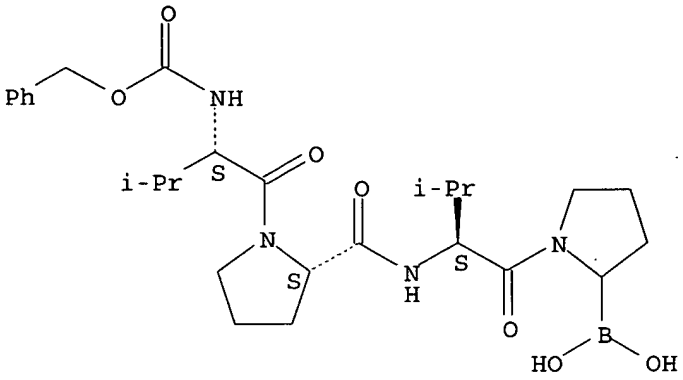
RN 623148-93-6 HCAPLUS
CN L-Prolinamide, 2-cyclohexylglycyl-N-[(1S)-2-(2-borono-1-pyrrolidinyl)-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

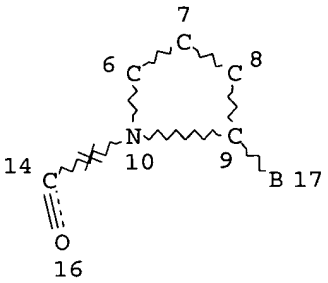


IT **623148-94-7**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FAP-activated FAP inhibitor; prodrugs of TASPI (Target-Activated Smart Protease Inhibitors) and TDSPI (Target-Directed Smart Protease Inhibitors))
RN 623148-94-7 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[(1S)-1-[(2-borono-1-pyrrolidinyl)carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



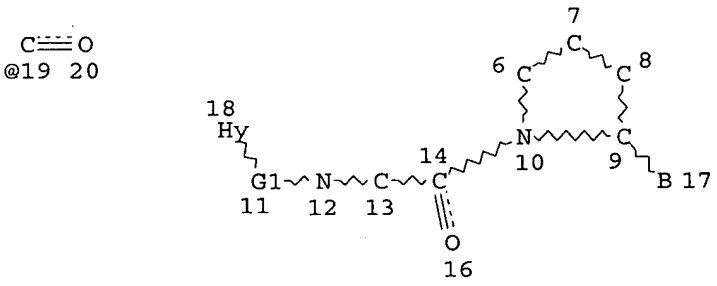
=> => d stat que
L7 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L9 304 SEA FILE=REGISTRY SSS FUL L7
L13 STR

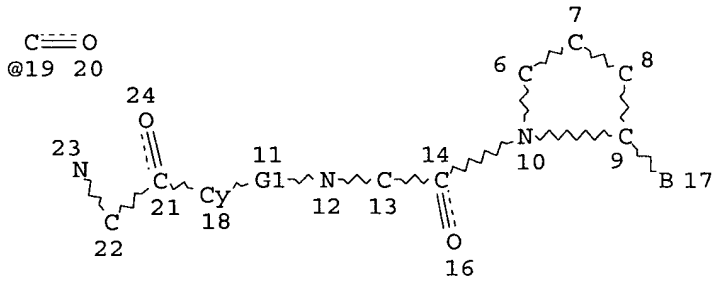


REP G1=(0-1) 19
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 18

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L14 59 SEA FILE=REGISTRY SUB=L9 SSS FUL L13
L20 STR



REP G1=(0-1) 19
NODE ATTRIBUTES:
NSPEC IS RC AT 12
NSPEC IS RC AT 13
NSPEC IS RC AT 14
NSPEC IS RC AT 21
NSPEC IS RC AT 22
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L21 3 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L23 56 SEA FILE=REGISTRY ABB=ON PLU=ON L14 NOT L21
L24 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

=> d ibib abs hitstr l24 1-2

L24 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451391 HCAPLUS
DOCUMENT NUMBER: 143:7824
TITLE: Preparation of heterocyclic boronic acid compounds and their pharmaceutical activity
INVENTOR(S): Campbell, David Alan; Winn, David
PATENT ASSIGNEE(S): Phenomix Corporation, USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

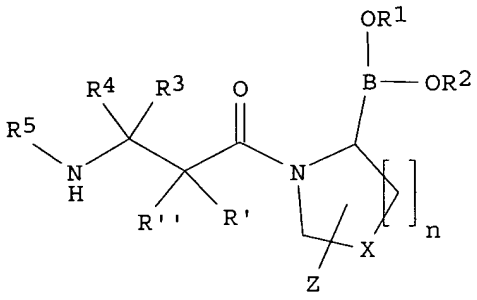
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005047297 A1 20050526 WO 2004-US37820 20041112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-519566P P 20031112
US 2004-557011P P 20040325
US 2004-592972P P 20040730

OTHER SOURCE(S): MARPAT 143:7824

GI



I

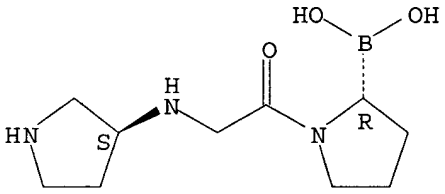
AB Preparation of dipeptidyl peptidase IV (DPP-IV)-inhibiting compds. I (n = 1-3; X = CH2, S, O, CF2, C(CH3)2; Z = H, halo, OH, (C1-6)alkoxy, (C1-12)alkyl, (C3-12)cycloalkyl, Ph, heteroaryl, where Ph and heteroaryl groups are optionally mono- or independently pluri-substituted with R7; optionally, X together with an adjacent ring carbon and Z form a fused cyclopropyl; and optionally, one of the bonds in the ring containing X is a double bond; and CR'R''; R1, R1 = H, boronic acid protecting group; R3, R4, R5 = H, (C1-12)alkyl, (C2-12)alkenyl, (C2-12)alkynyl, (C3-12)cycloalkyl, (C3-12)cycloalkenyl, etc.) are as described. Methods for preparing these compds., and methods for treating diabetes, especially Type II diabetes, and other related diseases are described using the compds. of I in pharmaceutical compns. which contain these compds. Pharmaceutical compns. which contain combinations of these compds. with other antidiabetic agents are also described herein.

IT **852329-62-5P 852329-66-9P 852329-88-5P**
852330-10-0P 852330-12-2P 852330-14-4P
852330-16-6P 852330-18-8P 852330-20-2P
852330-22-4P 852330-24-6P 852330-26-8P
852330-28-0P 852330-30-4P 852330-34-8P
852330-36-0P 852330-40-6P 852330-42-8P
852330-44-0P 852330-46-2P 852330-48-4P
852330-50-8P 852330-52-0P 852330-54-2P
852330-56-4P 852330-58-6P 852330-60-0P
852330-62-2P 852330-64-4P 852331-07-8P

852331-08-9P 852331-37-4P 852331-38-5P
852331-39-6P 852331-40-9P 852331-41-0P
852331-42-1P 852331-43-2P 852331-44-3P
852331-45-4P 852331-46-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic boronic acid compds. as antidiabetic agents)

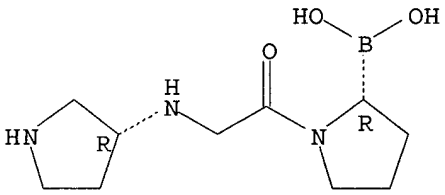
RN 852329-62-5 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3S)-3-pyrrolidinylamino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852329-66-9 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3R)-3-pyrrolidinylamino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

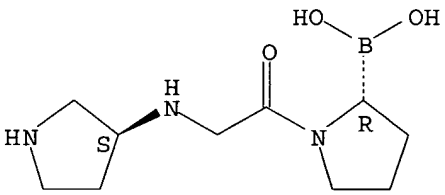


RN 852329-88-5 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3S)-3-pyrrolidinylamino]acetyl]-2-pyrrolidinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

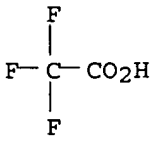
CRN 852329-62-5
CMF C10 H20 B N3 O3

Absolute stereochemistry.



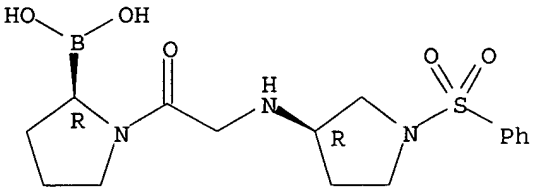
CM 2

CRN 76-05-1
CMF C2 H F3 O2



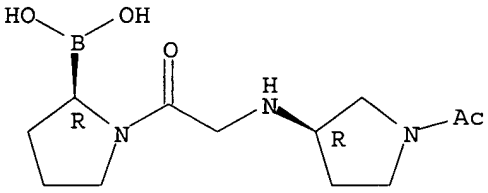
RN 852330-10-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(phenylsulfonyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



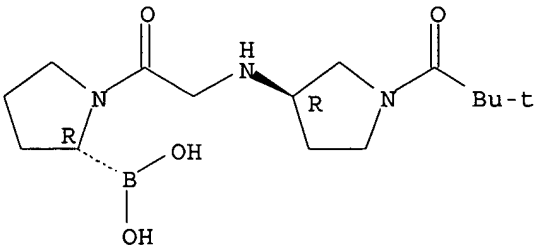
RN 852330-12-2 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-acetyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852330-14-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(2,2-dimethyl-1-oxopropyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

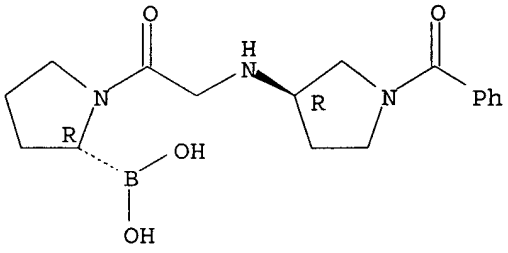
Absolute stereochemistry.



RN 852330-16-6 HCAPLUS

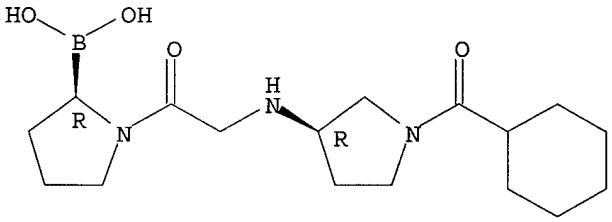
CN Boronic acid, [(2R)-1-[[[(3R)-1-benzoyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



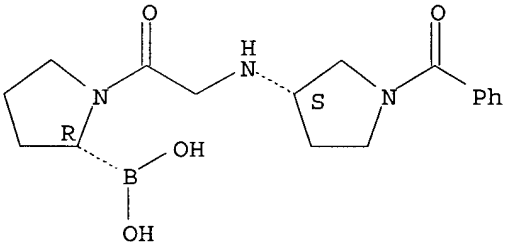
RN 852330-18-8 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(cyclohexylcarbonyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



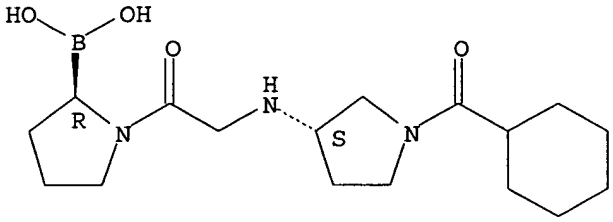
RN 852330-20-2 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-benzoyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



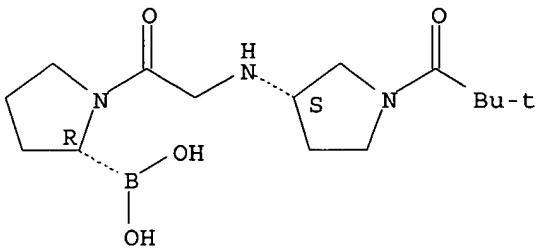
RN 852330-22-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-(cyclohexylcarbonyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



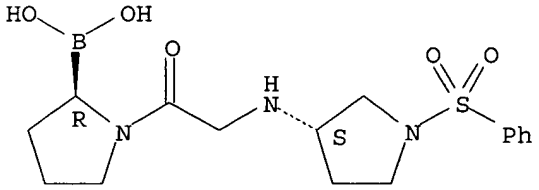
RN 852330-24-6 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-(2,2-dimethyl-1-oxopropyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



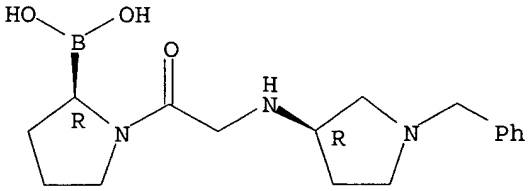
RN 852330-26-8 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-(phenylsulfonyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852330-28-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

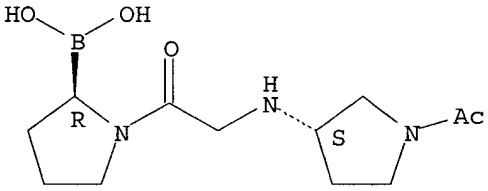
Absolute stereochemistry.



● 2 HCl

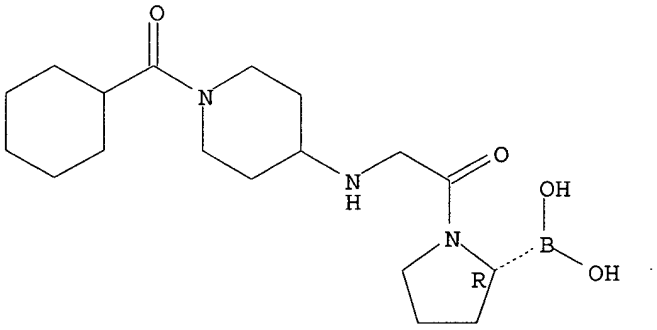
RN 852330-30-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-acetyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852330-34-8 HCAPLUS
CN Boronic acid, [(2R)-1-[[[1-(cyclohexylcarbonyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

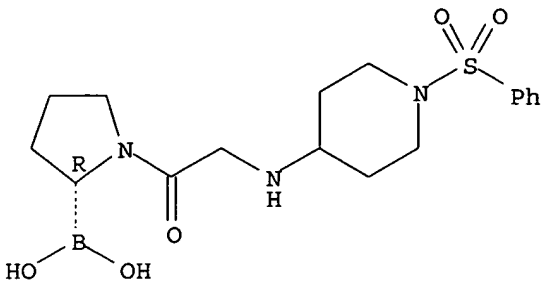
Absolute stereochemistry.



● HCl

RN 852330-36-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[1-(phenylsulfonyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

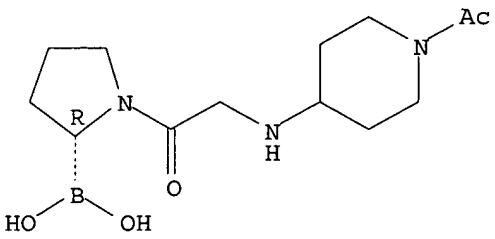
Absolute stereochemistry.



● HCl

RN 852330-40-6 HCAPLUS
CN Boronic acid, [(2R)-1-[[(1-acetyl-4-piperidinyl)amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

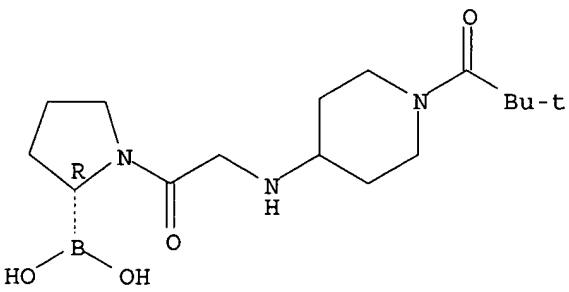
Absolute stereochemistry.



● HCl

RN 852330-42-8 HCAPLUS
CN Boronic acid, [(2R)-1-[[[1-(2,2-dimethyl-1-oxopropyl)-4-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

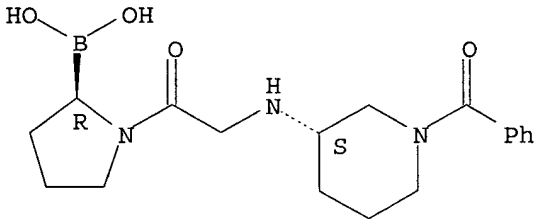
Absolute stereochemistry.



● HCl

RN 852330-44-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-benzoyl-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

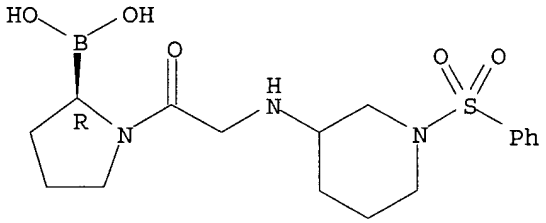
Absolute stereochemistry.



● HCl

RN 852330-46-2 HCAPLUS
CN Boronic acid, [(2R)-1-[[[1-(phenylsulfonyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

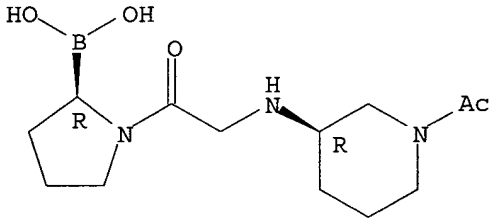
Absolute stereochemistry.



● HCl

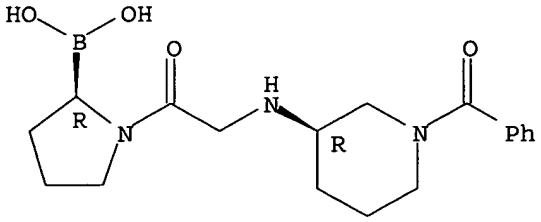
RN 852330-48-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-acetyl-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



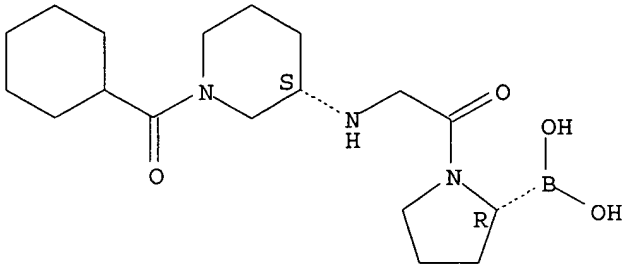
RN 852330-50-8 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-benzoyl-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852330-52-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-(cyclohexylcarbonyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

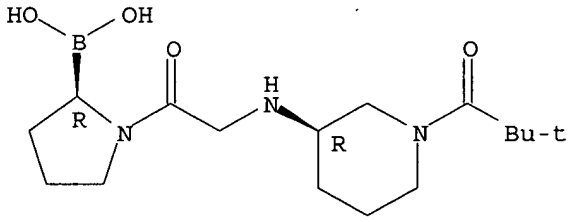
Absolute stereochemistry.



● HCl

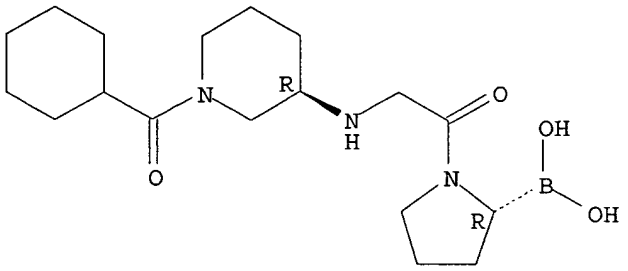
RN 852330-54-2 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(2,2-dimethyl-1-oxopropyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



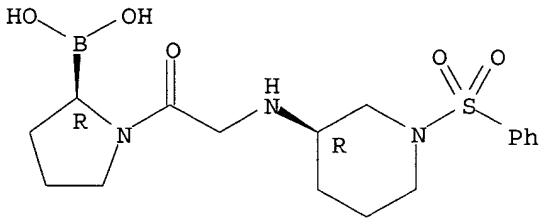
RN 852330-56-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(cyclohexylcarbonyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



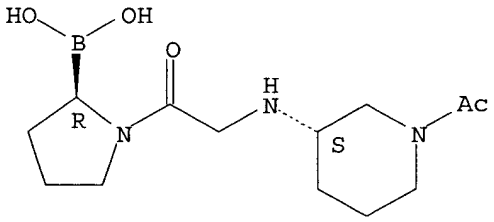
RN 852330-58-6 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-1-(phenylsulfonyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



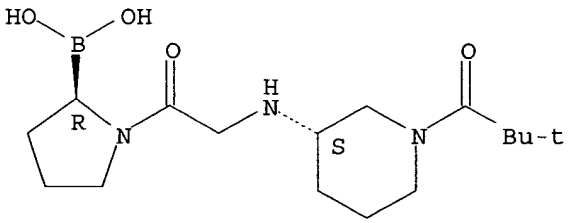
RN 852330-60-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-acetyl-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



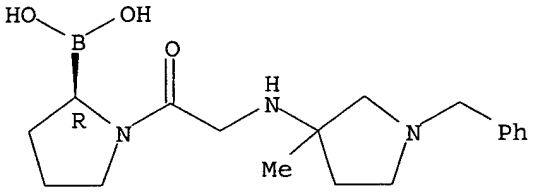
RN 852330-62-2 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-1-(2,2-dimethyl-1-oxopropyl)-3-piperidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



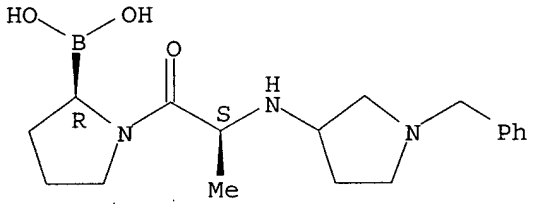
RN 852330-64-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[3-methyl-1-(phenylmethyl)-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852331-07-8 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-1-oxo-2-[[1-(phenylmethyl)-3-pyrrolidinyl]amino]propyl]-2-pyrrolidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

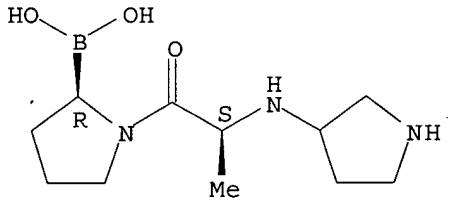
Absolute stereochemistry.



●2 HCl

RN 852331-08-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-1-oxo-2-(3-pyrrolidinylamino)propyl]-2-pyrrolidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

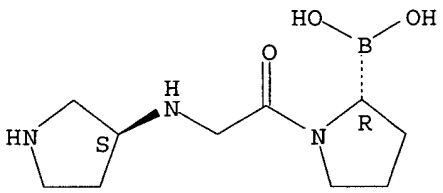
Absolute stereochemistry.



●2 HCl

RN 852331-37-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3S)-3-pyrrolidinylamino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

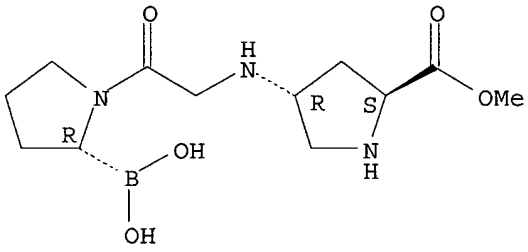
Absolute stereochemistry.



● HCl

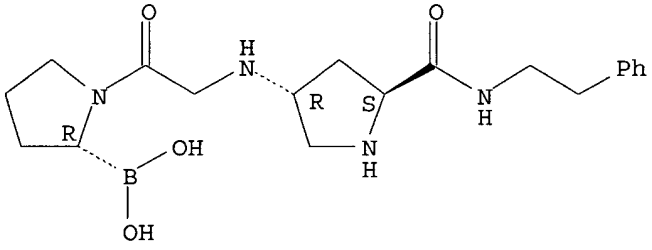
RN 852331-38-5 HCAPLUS
CN L-Proline, 4-[[2-[(2R)-2-borono-1-pyrrolidinyl]-2-oxoethyl]amino]-, 2-methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



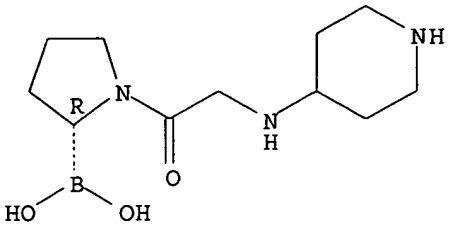
RN 852331-39-6 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R,5S)-5-[[(2-phenylethyl)amino]carbonyl]-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



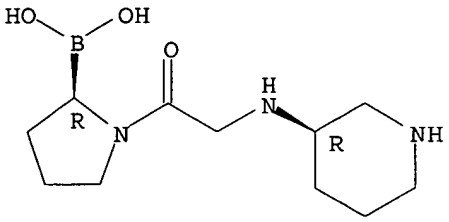
RN 852331-40-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(4-piperidinylamino)acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852331-41-0 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3R)-3-piperidinylamino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

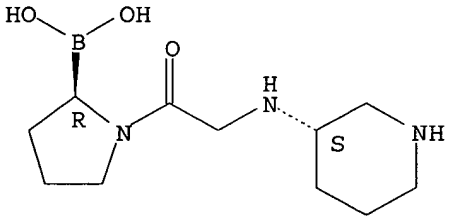
Absolute stereochemistry.



● HCl

RN 852331-42-1 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3S)-3-piperidinylamino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

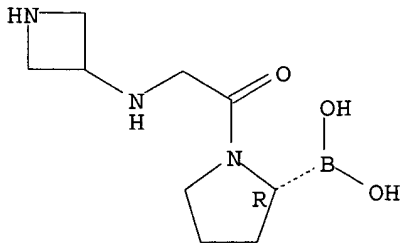
Absolute stereochemistry.



● HCl

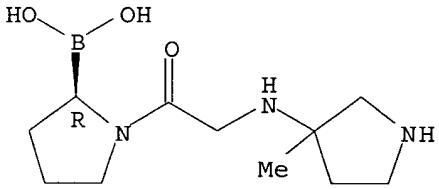
RN 852331-43-2 HCAPLUS
CN Boronic acid, [(2R)-1-[(3-azetidinylamino)acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852331-44-3 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3-methyl-3-pyrrolidinyl)amino]acetyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

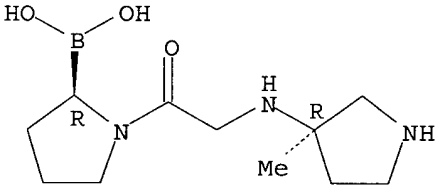
Absolute stereochemistry.



● HCl

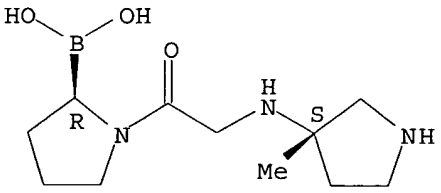
RN 852331-45-4 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3R)-3-methyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 852331-46-5 HCAPLUS
CN Boronic acid, [(2R)-1-[[[(3S)-3-methyl-3-pyrrolidinyl]amino]acetyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



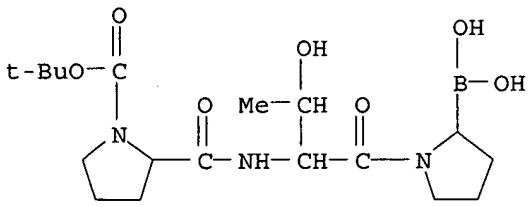
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:231733 HCAPLUS
DOCUMENT NUMBER: 112:231733
TITLE: Inhibition of IgA1 proteinases from Neisseria gonorrhoeae and Hemophilus influenzae by peptide prolyl boronic acids
AUTHOR(S): Bachovchin, William W.; Plaut, Andrew G.; Flentke, George R.; Lynch, Mary; Kettner, Charles A.
CORPORATE SOURCE: Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SOURCE: Journal of Biological Chemistry (1990), 265(7), 3738-43
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

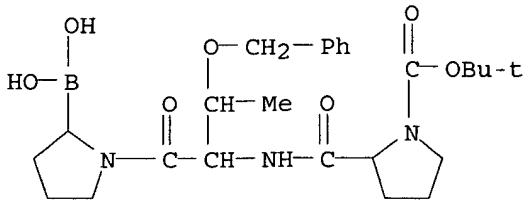
AB The α-aminoboronic acid analog of proline was synthesized and incorporated into a number of peptides as the C-terminal residue. These peptide prolyl boronic acids are potent inhibitors of both the type 1 and type 2 IgA proteinases from N. gonorrhoeae and H. influenzae, but not of the functionally similar IgA proteinase from Streptococcus sanguis. The best inhibitors synthesized thus far have Ki values in the nanomolar range (4.0 to 60 nM). These results indicate that the N. gonorrhoeae and the H. influenzae enzymes belong to the serine protease family of proteolytic enzymes, whereas that from S. sanguis does not. As a group, the IgA proteinases have been noted for their remarkable specificity; thus, the peptide prolyl boronic acids reported here are the 1st small synthetic mol. to exhibit a relatively high affinity for the active site of an IgA proteinase and are therefore the 1st to yield some insight into the active site structure and specificity requirements of these enzymes.

IT **127292-34-6P 127292-35-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and inhibition kinetics with IgA1 proteinases)

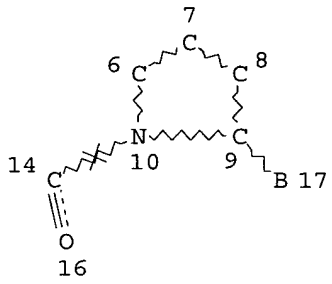
RN 127292-34-6 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[1-[(2-borono-1-pyrrolidinyl)carbonyl]-2-hydroxypropyl]amino]carbonyl]-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 127292-35-7 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[1-[(2-borono-1-pyrrolidinyl)carbonyl]-2-(phenylmethoxy)propyl]amino]carbonyl]-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



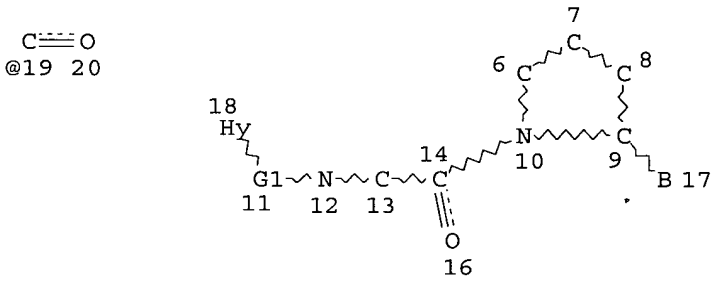
=> => d stat que l28
L7 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

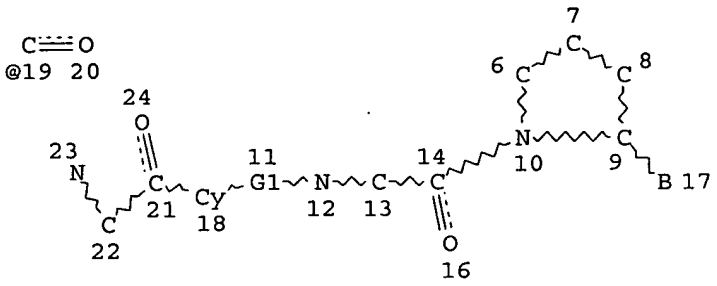
STEREO ATTRIBUTES: NONE
L9 304 SEA FILE=REGISTRY SSS FUL L7
L13 STR



REP G1=(0-1) 19
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 18
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L14 59 SEA FILE=REGISTRY SUB=L9 SSS FUL L13
L20 STR



REP G1=(0-1) 19
NODE ATTRIBUTES:
NSPEC IS RC AT 12
NSPEC IS RC AT 13
NSPEC IS RC AT 14
NSPEC IS RC AT 21
NSPEC IS RC AT 22
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L21 3 SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L22 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L21
L23 56 SEA FILE=REGISTRY ABB=ON PLU=ON L14 NOT L21
L24 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L25 245 SEA FILE=REGISTRY ABB=ON PLU=ON L9 NOT (L21 OR L23)
L26 234 SEA FILE=HCAPLUS ABB=ON PLU=ON L25
L27 232 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 NOT (L22 OR L24)
L28 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND PD=<OCTOBER 24, 1991

=>
=>

=> d ibib abs hitstr l28 1-5

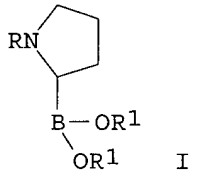
L28 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:152411 HCAPLUS
DOCUMENT NUMBER: 116:152411
TITLE: Preparation of proline boronic acid analogs as inhibitors of dipeptidyl aminopeptidase IV
INVENTOR(S): Bachovchin, William W.; Plaut, Andrew G.; Flentke, George R.
PATENT ASSIGNEE(S): New England Medical Center Hospitals, Inc., USA; Tufts University
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9116339	A1	19911031	WO 1991-US2519	19910412
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2080474	AA	19911015	CA 1991-2080474	19910412 <--
EP 528858	A1	19930303	EP 1991-908724	19910412
EP 528858	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05508624	T2	19931202	JP 1991-508358	19910412
AT 148130	E	19970215	AT 1991-908724	19910412
ES 2099158	T3	19970516	ES 1991-908724	19910412
US 5462928	A	19951031	US 1993-93302	19930715
PRIORITY APPLN. INFO.:			US 1990-510274 A	19900414
			WO 1991-US2519 W	19910412
			US 1991-781552 B1	19911022

OTHER SOURCE(S): MARPAT 116:152411

GI



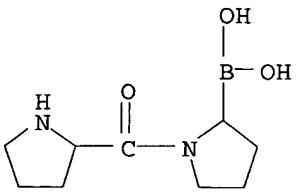
I

AB The title compds., e.g., H-X-Pro-Y-boroPro [boroPro designating a proline residue with the CO2H group replaced by a B(OH)2 group; X, Y = amino acid residue, including Pro], inhibitors of dipeptidyl aminopeptidase IV and therefore useful as inhibitors of HIV-1, are prepared by condensation of the appropriate amino acid or peptide with boroProline pinacol (I; R = H, R1R1 = CMe2CMe2) (II) via the mixed anhydride followed by deprotection. E.g., H-Ala-boroPro (I; R = H-Ala, R1 = H) (III) was prepared by mixed anhydride coupling of BOC-Ala-OH with II and subsequent deprotection. In an in vitro study using A3.5 cells infected with HIV-1 IIIB, III suppressed HIV (no concentration given) in a manner similar to the anti-HIV effect of AZT at 1 μM.

IT **133745-65-0P 139649-82-4P 139649-83-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as inhibitor of dipeptidyl aminopeptidase IV)

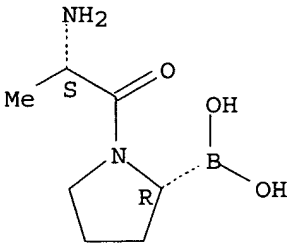
RN 133745-65-0 HCAPLUS

CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



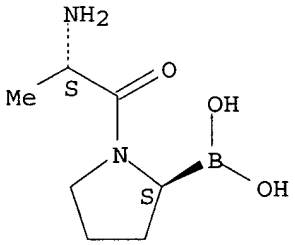
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 139649-83-5 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

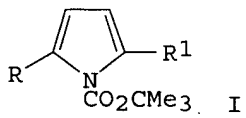
Absolute stereochemistry.



L28 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1991:583003 HCAPLUS
DOCUMENT NUMBER:	115:183003
TITLE:	N-Protected pyrrole derivatives substituted for metal-catalyzed cross-coupling reactions
AUTHOR(S):	Martina, Stefano; Enkelmann, Volker; Wegner, Gerhard; Schlueter, Arnulf Dieter
CORPORATE SOURCE:	Max-Planck-Inst. Polymerforsch., Mainz, D-6500, Germany
SOURCE:	Synthesis (**1991**), (8), 613-15 CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 115:183003

GI



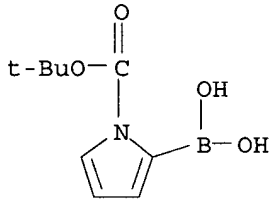
I

AB The 1-tert-butoxycarbonylpyrroles I [R = H, Br, R1 = B(OMe)2, B(OH)2, SnMe3; R = R1 = Br, B(OMe)2, SnMe3] were prepared from I (R = R1 = H). Thus, I (R = R1 = H) was treated with NBS in THF to give 61% I (R = R1 = Br), which on lithiation with BuLi in THF and treatment with Me3SnCl gave 71% I (R = Br, R1 = SnMe3).

IT **135884-31-0P 135884-33-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

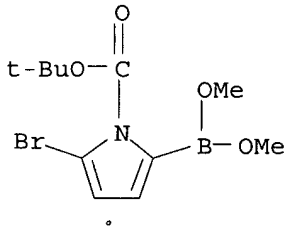
RN 135884-31-0 HCAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-borono-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 135884-33-2 HCAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-bromo-5-(dimethoxyboryl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L28 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:515137 HCAPLUS

DOCUMENT NUMBER: 115:115137

TITLE: Polypyrrole: towards the development of a chemical synthesis

AUTHOR(S): Martina, S.; Enkelmann, V.; Schlueter, A. D.; Wegner, G.

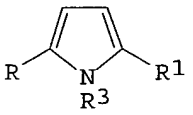
CORPORATE SOURCE: Max-Planck-Inst. Polymerforsch., Mainz, D-6500, Germany

SOURCE: Synthetic Metals (**1991**), 41(1-2), 403-6
CODEN: SYMEDZ; ISSN: 0379-6779

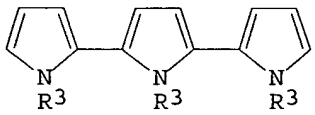
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



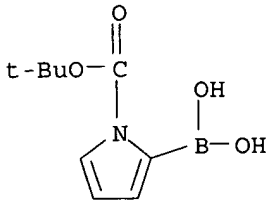
II

AB Pyrrole monomers having the structure I (where R, R1 = Br or B(OR2); R2 = H or alkyl; R3 = a tert-butoxycarbonyl protecting group) were prepared and their Pd-catalyzed coupling reactions were studied in order to evaluate whether structurally well-defined poly(2,5-pyrrole) could be obtained by a polymerization reaction of aromatic nuclei containing both a boronic acid function and substituted Br. Although coupling was possible in principle, deboronification was a serious side reaction which could not be suppressed. However, a model coupling reaction of I (R = H; R1 = Me3Sn) with I (R = R1 = Br) yielded .apprx.30% trimer (II). Single crystal x-ray diffraction anal. of Br-containing dimers and trimers and II proved that the pyrrole rings were not coplanar.

IT **135884-31-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling reaction of, with dibromopyrrole derivative, as model for poly(pyrrole) preparation)

RN 135884-31-0 HCAPLUS

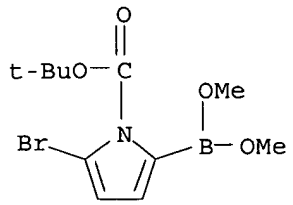
CN 1H-Pyrrole-1-carboxylic acid, 2-borono-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



IT **135884-33-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling reaction of, with dibromopyrrole derivative, as model reaction for poly(pyrrole) preparation)

RN 135884-33-2 HCAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-bromo-5-(dimethoxyboryl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L28 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:205351 HCAPLUS

DOCUMENT NUMBER: 114:205351

TITLE: Inhibition of dipeptidyl aminopeptidase IV (DP-IV) by Xaa-boroPro dipeptides and use of these inhibitors to examine the role of DP-IV in T-cell function

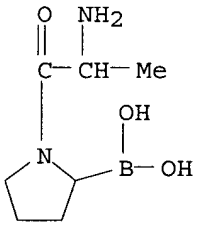
AUTHOR(S): Flentke, George R.; Munoz, Eduardo; Huber, Brigitte T.; Plaut, Andrew G.; Kettner, Charles A.; Bachovchin, William W.

CORPORATE SOURCE: Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1991**), 88(4), 1556-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

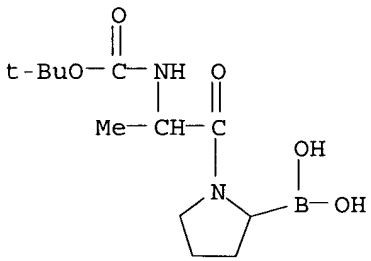
AB Dipeptidyl peptidase IV (DP-IV; dipeptidyl-peptide hydrolase, EC 3.4.14.5) is a serine protease with a specificity for cleaving Xaa-Pro dipeptides from polypeptides and proteins. It is found in a variety of mammalian cells and tissues, including those of lymphoid origin where it is found specifically on the surface of CD4+ T cells. Although the functional significance of this enzyme has not been established, a role in T-cell activation and immune regulation has been proposed. Here is reported that Ala-boroPro and Pro-boroPro, where boroPro is the α-amino boronic acid analog of proline, are potent and specific inhibitors of DP-IV, having Ki values in the nanomolar range. Blocking the N terminus of Ala-boroPro abolishes the affinity of this inhibitor for DP-IV, while removal of the N-terminal residue, to give boroPro, reduces the affinity for DP-IV by 5 orders of magnitude. The dipeptide boronic acids exhibit slow-binding kinetics, while boroPro does not. Low concns. of Pro-boroPro inhibit antigen-induced proliferation and interleukin 2 production in murine T-cell lines but do not inhibit the response of these T cells to the mitogen Con A. Thus, DP-IV plays a role in antigen-induced, but not mitogen-induced, activation of T lymphocytes.

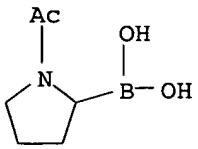
IT **127292-29-9 127292-30-2 133745-65-0**
RL: BIOL (Biological study)
(antigen- vs. mitogen-induced T-lymphocyte activation inhibition by, dipeptidyl peptidase IV in)

RN 127292-29-9 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

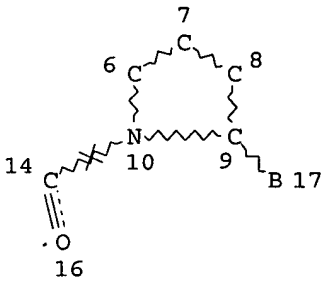


RN 127292-30-2 HCAPLUS
CN Carbamic acid, [2-(2-borono-1-pyrrolidinyl)-1-methyl-2-oxoethyl]-, C-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)





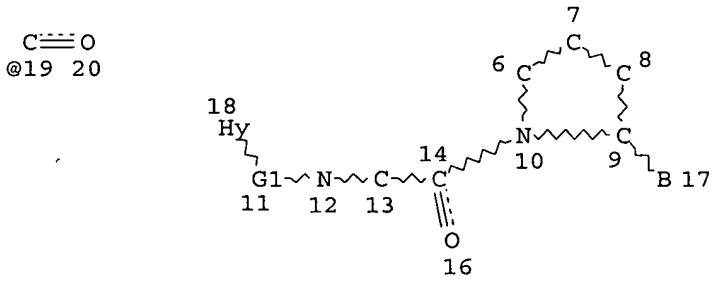
=> => d stat que l36
L7 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L9 304 SEA FILE=REGISTRY SSS FUL L7
L13 STR

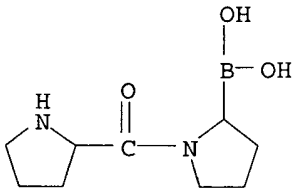


REP G1=(0-1) 19
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 18
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L14 59 SEA FILE=REGISTRY SUB=L9 SSS FUL L13

RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

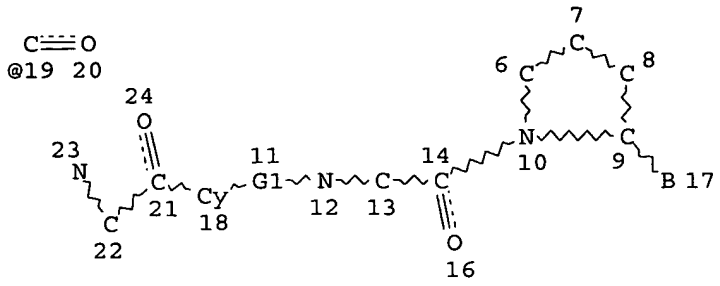


L28 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:545119 HCAPLUS
DOCUMENT NUMBER: 109:145119
TITLE: Kinetic properties of the binding of α-lytic protease to peptide boronic acids
AUTHOR(S): Kettner, Charles A.; Bone, Roger; Agard, David A.; Bachovchin, William W.
CORPORATE SOURCE: Cent. Res. Dev. Dep., E. I. du Pont de Nemours and Co., Wilmington, DE, 19898, USA
SOURCE: Biochemistry (**1988**), 27(20), 7682-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The kinetic parameters for peptide boronic acids in their interaction with α-lytic protease were determined and found to be similar to those of other serine proteases (Kettner, C.; Shenvi, A. B., 1984). α-Lytic protease hydrolyzes substrates with either alanine or valine in the P1 site and has a preference for substrates with a P1 alanine. The most effective inhibitors are tri- and tetrapeptide analogs that have a -boroVal-OH [where the carbonyl group of valine is replaced by B(OH)2] residue in the P1 site. At pH 7.5, MeOSuc-Ala-Ala-Pro-boroVal-OH has a Ki of 6.4 nM and Boc-Ala-Pro-boroVal-OH has a Ki of 0.35 nM. Ac-boroVal-OH and Ac-Pro-boroVal-OH are 220,000- and 500-fold less effective, resp., than the tetrapeptide analog. The kinetic properties of the tri- and tetrapeptide analogs are consistent with the mechanism for slow-binding inhibition, while the less effective inhibitors are simple competitive inhibitors. MeOSuc-Ala-Ala-Pro-boroAla-OH is a simple competitive inhibitor with a Ki of 67 nM at pH 7.5. Other peptide boronic acids, which are analogs of nonsubstrates, are less effective than substrate analogs but still are effective competitive inhibitors. For example, MeOSuc-Ala-Ala-Pro-boroPhe-OH has a Ki of 0.54 μM although substrates with a phenylalanine (Phe) in the P1 position are not hydrolyzed. Binding for boronic acid analogs of both substrate and nonsubstrate analogs is pH-dependent with higher affinity near pH 7.5. Similar binding properties have been observed for pancreatic elastase. Both enzymes have almost identical requirements for an extended peptide inhibitor sequence in order to exhibit highly effective binding and slow-binding characteristics. Both enzymes have a greater than expected affinity for the nonsubstrate analog terminating in boroPhe-OH.

IT **116150-20-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and kinetics of α-lytic protease inhibition by)
RN 116150-20-0 HCAPLUS
CN Boronic acid, (1-acetyl-2-pyrrolidinyl)- (9CI) (CA INDEX NAME)

L20 STR



REP G1=(0-1) 19
NODE ATTRIBUTES:
NSPEC IS RC AT 12
NSPEC IS RC AT 13
NSPEC IS RC AT 14
NSPEC IS RC AT 21
NSPEC IS RC AT 22
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L21	3	SEA FILE=REGISTRY SUB=L14 SSS FUL L20
L22	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L21
L23	56	SEA FILE=REGISTRY ABB=ON PLU=ON L14 NOT L21
L24	2	SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L25	245	SEA FILE=REGISTRY ABB=ON PLU=ON L9 NOT (L21 OR L23)
L26	234	SEA FILE=HCAPLUS ABB=ON PLU=ON L25
L27	232	SEA FILE=HCAPLUS ABB=ON PLU=ON L26 NOT (L22 OR L24)
L28	5	SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND PD=<OCTOBER 24, 1991
L29	97	SEA FILE=HCAPLUS ABB=ON PLU=ON ("BACHOVCHIN W W"/AU OR "BACHOVCHIN WILLIAM"/AU OR "BACHOVCHIN WILLIAM W"/AU OR "BACHOVCHIN WILLIAM WALTER"/AU)
L30	99	SEA FILE=HCAPLUS ABB=ON PLU=ON "PLAUT A"/AU OR "PLAUT A G"/AU OR ("PLAUT ANDREW"/AU OR "PLAUT ANDREW G"/AU)
L31	28	SEA FILE=HCAPLUS ABB=ON PLU=ON ("FLENTKE G R"/AU OR "FLENTKE GEORGE"/AU OR "FLENTKE GEORGE F"/AU OR "FLENTKE GEORGE R"/AU OR "FLENTKE GEORGE ROBERT"/AU)
L32	1	SEA FILE=HCAPLUS ABB=ON PLU=ON (L29 AND L30 AND L31) NOT (L22 OR L24 OR L28)
L33	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND (L30 OR L31)
L34	4	SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L31
L35	21	SEA FILE=HCAPLUS ABB=ON PLU=ON (L29 OR L30 OR L31) AND L27
L36	21	SEA FILE=HCAPLUS ABB=ON PLU=ON (L32 OR L33 OR L34 OR L35) NOT (L22 OR L24 OR L28)

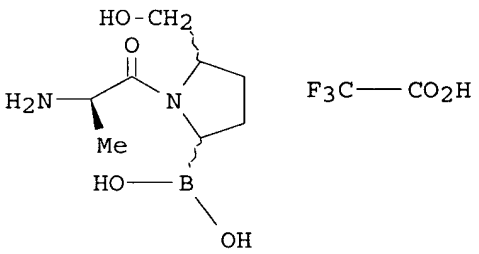
=> d ibib abs hitstr l36 1-21

L36 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:984020 HCAPLUS
DOCUMENT NUMBER: 143:279447
TITLE: Inhibitors of dipeptidyl peptidase IV, their

preparation, and their therapeutic use
INVENTOR(S): **Bachovchin, William W.**; Lai, Hung-Sen; Wu, Wengen
PATENT ASSIGNEE(S): Trustees of Tufts College, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082348	A2	20050909	WO 2005-US6128	20050223
WO 2005082348	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005203027	A1	20050915	US 2005-65001	20050223
PRIORITY APPLN. INFO.:			US 2004-547227P P	20040223
			US 2004-599336P P	20040806

OTHER SOURCE(S): MARPAT 143:279447
GI



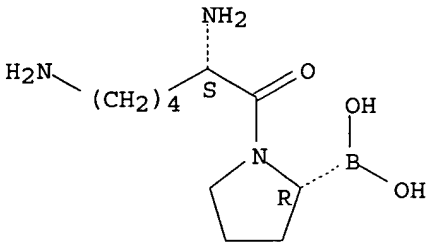
I

AB The invention relates to inhibitors of post-proline cleaving enzymes, e.g. inhibitors of dipeptidyl peptidase IV, as well as pharmaceutical compns. thereof, and methods of using such inhibitors. In particular, the inhibitors of the invention are improved over those in the prior art by selection of particular classes of sidechains in the P1 and/or P2 position of the inhibitor that contain a carboxylic acid moiety. The compds. of the invention can have a better therapeutic index, owing in part to reduced toxicity and/or improved specificity for the targeted protease. Preparation of e.g. I is included.

IT **783282-58-6 857507-69-8 864074-51-1**
864074-72-6
RL: PAC (Pharmacological activity); BIOL (Biological study)
(dipeptidyl peptidase IV inhibitors, and therapeutic use)

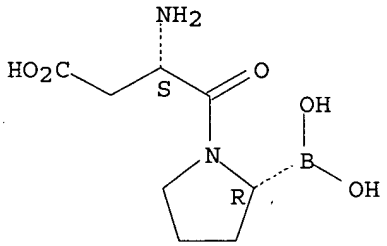
RN 783282-58-6 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



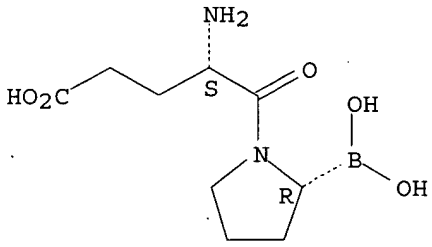
RN 857507-69-8 HCAPLUS
CN 1-Pyrrolidinebutanoic acid, β-amino-2-borono-γ-oxo-, (βS,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



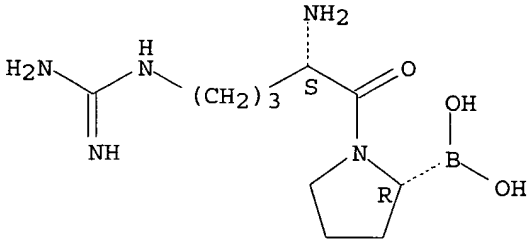
RN 864074-51-1 HCAPLUS
CN 1-Pyrrolidinepentanoic acid, γ-amino-2-borono-δ-oxo-, (γS,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864074-72-6 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

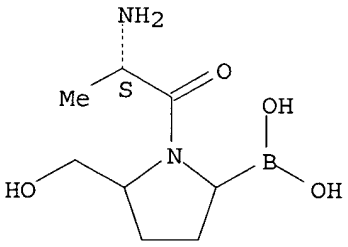


IT **864074-58-8P 864074-63-5P 864074-67-9P**
864074-71-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dipeptidyl peptidase IV inhibitors, and therapeutic use)
RN 864074-58-8 HCAPLUS
CN Boronic acid, [1-[(2S)-2-amino-1-oxopropyl]-5-(hydroxymethyl)-2-pyrrolidinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

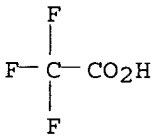
CRN 864074-57-7
CMF C8 H17 B N2 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

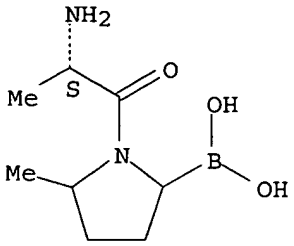


RN 864074-63-5 HCAPLUS
CN Boronic acid, [1-[(2S)-2-amino-1-oxopropyl]-5-methyl-2-pyrrolidinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

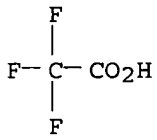
CRN 864074-62-4
CMF C8 H17 B N2 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

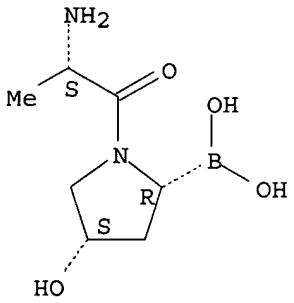


RN 864074-67-9 HCAPLUS
CN Boronic acid, [(2R,4S)-1-[(2S)-2-amino-1-oxopropyl]-4-hydroxy-2-pyrrolidinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

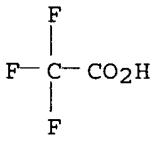
CRN 864074-66-8
CMF C7 H15 B N2 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

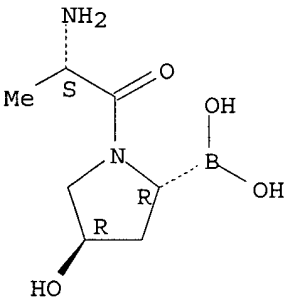


RN 864074-71-5 HCAPLUS
CN Boronic acid, [(2R,4R)-1-[(2S)-2-amino-1-oxopropyl]-4-hydroxy-2-pyrrolidinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

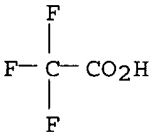
CRN 864074-70-4
CMF C7 H15 B N2 O4

Absolute stereochemistry.

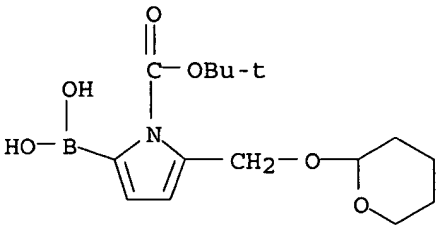


CM 2

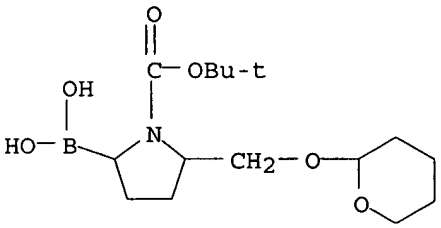
CRN 76-05-1
CMF C2 H F3 O2



IT **864074-54-4P 864074-55-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dipeptidyl peptidase IV inhibitors, and therapeutic use)
RN 864074-54-4 HCAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-borono-5-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, C-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 864074-55-5 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-borono-5-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, C-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L36 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:419663 HCAPLUS
DOCUMENT NUMBER: 143:115782
TITLE: Autochelation in Dipeptide Boronic Acids: pH-Dependent Structures and Equilibria of Asp-boroPro and His-boroPro by NMR Spectroscopy
AUTHOR(S): Sudmeier, James L.; Zhou, Yuhong; Lai, Jack H.; Maw, Hlaing H.; Wu, Wengen; **Bachovchin, William W.**
CORPORATE SOURCE: Department of Biochemistry, Tufts University School of Medicine, Boston, MA, 02111, USA
SOURCE: Journal of the American Chemical Society (2005), 127(22), 8112-8119
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

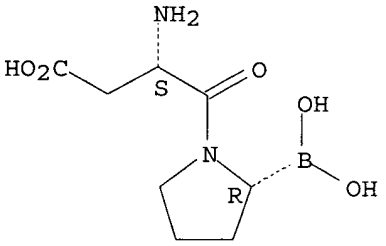
AB Many dipeptide boronic acids of the type H2N-X-Y-B(OH)2 [X = Asp, His; Y = Pro with carboxy group replaced by B(OH)2] are potent protease inhibitors. Because of the great mutual B-N affinity, cyclization through the N- and B-termini, forming six-membered rings, is a common occurrence at neutral pH and higher where the terminal amino group is unprotonated. This work reports the discovery that when X, the N-terminal amino acid, contains a side chain having a functional group with boron affinity and suitable geometry, addnl. cyclization in the form of bidentate intramol. chelation or "autochelation" may occur, predominantly at mid pH. NMR studies of two compds., L-Aspartyl-L-boroProline (Asp-boroPro) and L-Histidyl-L-boroProline (His-boroPro), are reported here from pH 0.5 to pH 12 by 1H, 15N, 13C, and 11B NMR. Both of these previously unreported autochelates contain two fused six-membered rings, cis-proline, chiral boron, and -NH2+ protons in slow exchange with water, even at 25° and pH as high as 4. Using microscopic acid-base equilibrium consts., it is shown that at high pH (>8 for Asp-boroPro and >10 for His-boroPro) hydroxide competes with the side chains for boron, reducing the chelates from bidentate to

monodentate. At low pH (<0.5), proton competition for N-terminal nitrogens causes both compds. to become noncyclic. High chelate stability causes a reduction of the apparent acidic dissociation constant of the protonated
N-terminal amino group greater than eight units. In the His-boroPro autochelate, imidazolate anion is produced at the extraordinarily low pH value of .apprx.9.

IT **857507-70-1 857507-73-4**
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); FORM (Formation, nonpreparative); PROC (Process); RACT (Reactant or reagent)
(NMR studies of pH-dependent structures and equilibrium in autochelation of dipeptides Asp-boroPro and His-boroPro)

RN 857507-70-1 HCAPLUS
CN 1-Pyrrolidinebutanoic acid, β-amino-2-borono-γ-oxo-, conjugate monoacid, (βS,2R)- (9CI) (CA INDEX NAME)

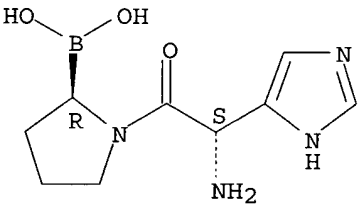
Absolute stereochemistry.



● H^+

RN 857507-73-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-amino-1H-imidazol-4-ylacetyl]-2-pyrrolidinyl]-, conjugate diacid (9CI) (CA INDEX NAME)

Absolute stereochemistry.



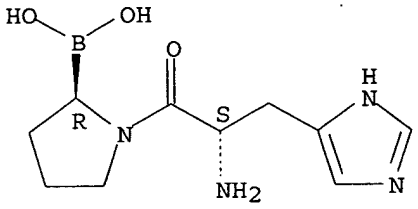
●2 H^+

IT **738561-50-7 857507-69-8**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(NMR studies of pH-dependent structures and equilibrium in autochelation of dipeptides Asp-boroPro and His-boroPro)

RN 738561-50-7 HCAPLUS

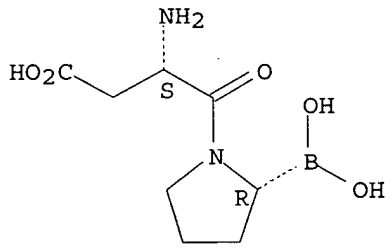
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-(1H-imidazol-4-yl)-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 857507-69-8 HCAPLUS
CN 1-Pyrrolidinebutanoic acid, β-amino-2-borono-γ-oxo-, (βS,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:434583 HCAPLUS
DOCUMENT NUMBER: 139:17584
TITLE: Peptidomimetic inhibitors of post-proline cleaving enzymes
INVENTOR(S): **Bachovchin, William W.**
PATENT ASSIGNEE(S): Trustees of Tufts College, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045977	A2	20030605	WO 2002-US38053	20021126
WO 2003045977	A3	20040513		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

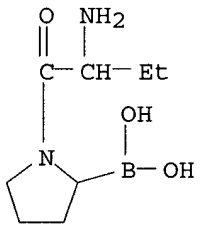
CA 2468192	AA	20030605	CA 2002-2468192		20021126
AU 2002357767	A1	20030610	AU 2002-357767		20021126
EP 1469873	A2	20041027	EP 2002-792306		20021126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005514377	T2	20050519	JP 2003-547426		20021126
US 2005070482	A1	20050331	US 2004-496706		20041022
PRIORITY APPLN. INFO.:			US 2001-333519P	P	20011126
			US 2002-405530P	P	20020823
			WO 2002-US38053	W	20021126

OTHER SOURCE(S): MARPAT 139:17584

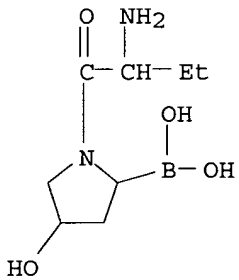
AB The invention relates to inhibitors of post-proline cleaving enzymes, such as inhibitors of dipeptidyl peptidase IV, as well as pharmaceutical compns. thereof, and methods for using such inhibitors. In particular, the inhibitors of the present invention are improved over those in the prior art by selection of particular classes of sidechains in the P1 and/or P2 position of the inhibitor. The compds. of the present invention can have a better therapeutic index, owing in part to reduced toxicity and/or improved specificity for the targeted protease.

IT **536994-18-0P 536994-19-1P 536994-20-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetic inhibitors of post-proline cleaving enzymes)

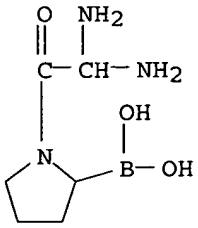
RN 536994-18-0 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxobutyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



RN 536994-19-1 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxobutyl)-4-hydroxy-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

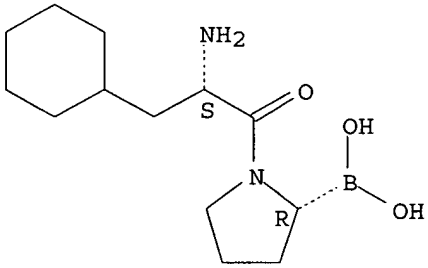


RN 536994-20-4 HCAPLUS
CN Boronic acid, [1-(diaminoacetyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



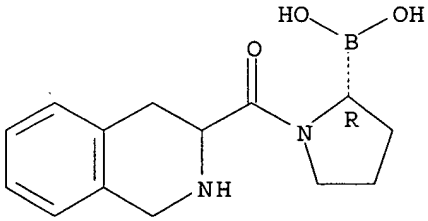
IT **536994-15-7 536994-16-8 536994-17-9**
536994-25-9 536994-26-0 536994-27-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidomimetic inhibitors of post-proline cleaving enzymes)
RN 536994-15-7 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-cyclohexyl-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



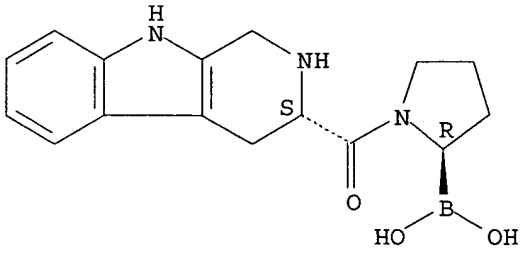
RN 536994-16-8 HCAPLUS
CN Boronic acid, [(2R)-1-[(1,2,3,4-tetrahydro-3-isoquinolinyl)carbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

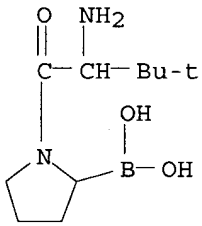


RN 536994-17-9 HCAPLUS
CN Boronic acid, [(2R)-1-[[(3S)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-3-yl]carbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

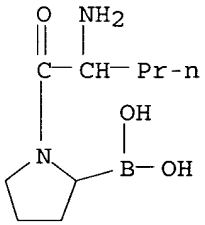
Absolute stereochemistry.



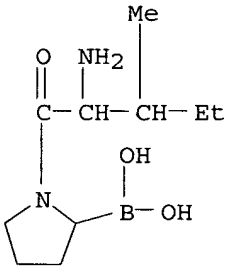
RN 536994-25-9 HCAPLUS
CN Boronic acid, [1-(2-amino-3,3-dimethyl-1-oxobutyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



RN 536994-26-0 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopentyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



RN 536994-27-1 HCAPLUS
CN Boronic acid, [1-(2-amino-3-methyl-1-oxopentyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



L36 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:434292 HCAPLUS
DOCUMENT NUMBER: 139:17583
TITLE: Methods for treating autoimmune disorders, and reagents related thereto
INVENTOR(S): **Bachovchin, William W.**; Kuchroo, Vijay K.
PATENT ASSIGNEE(S): Trustees of Tufts College, USA; Brigham and Women's Hospital
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045228	A2	20030605	WO 2002-US38347	20021126
WO 2003045228	C2	20040916		
WO 2003045228	A3	20041021		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2466870	AA	20030605	CA 2002-2466870	20021126
AU 2002360453	A1	20030610	AU 2002-360453	20021126
EP 1487471	A2	20041222	EP 2002-795710	20021126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005511636	T2	20050428	JP 2003-546737	20021126
US 2005070459	A1	20050331	US 2004-496627	20041115
PRIORITY APPLN. INFO.:			US 2001-333691P P	20011126
			WO 2002-US38347 W	20021126

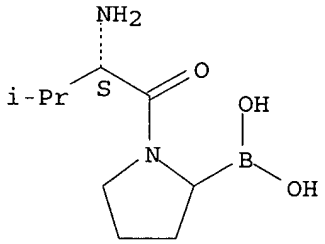
OTHER SOURCE(S): MARPAT 139:17583

AB The invention generally relates to improved methods for treatment or prophylaxis in animal subjects (including humans) of autoimmune disorders including Type 1 diabetes, septic shock, multiple sclerosis, inflammatory bowel disease (IBD) and Crohn's disease.

IT **215923-24-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating autoimmune disorders with peptidomimetic dipeptidylpeptidase IV inhibitor)

RN 215923-24-3 HCAPLUS
CN Boronic acid, [1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:655941 HCAPLUS
DOCUMENT NUMBER: 131:281562
TITLE: Peptide-based multivalent compounds for crosslinking immune cell receptors, and uses thereof
INVENTOR(S): **Bachovchin, William W.**
PATENT ASSIGNEE(S): Trustees of Tufts College, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 671,756, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5965532	A	19991012	US 1997-837305	19970411
CA 2258038	AA	19980108	CA 1997-2258038	19970627
WO 9800439	A2	19980108	WO 1997-US11279	19970627
WO 9800439	A3	20000824		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9737927	A1	19980121	AU 1997-37927	19970627
AU 739241	B2	20011004		
EP 938498	A1	19990901	EP 1997-934862	19970627
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE				
CN 1229414	A	19990922	CN 1997-195969	19970627
JP 2000515500	T2	20001121	JP 1998-504344	19970627
US 6875737	B1	20050405	US 1999-289321	19990409
US 2005202027	A1	20050915	US 2005-30591	20050106

PRIORITY APPLN. INFO.:

US 1996-671756	B2	19960628
US 1996-77180P	P	19960628
US 1997-837305	A	19970411
WO 1997-US11279	W	19970627
US 1999-289321	A1	19990409

OTHER SOURCE(S): MARPAT 131:281562

AB Synthetic crosslinking homobivalent and heterobivalent compds. have been designed and developed. These compds. are low in mol. weight, have antagonistic or agonistic activity, and induce the association between two identical or similar natural receptors (homobivalent compds.) or induce

the association between two different natural receptors (heterobivalent compds.). The preparation and immunosuppressant/immunostimulatory activity of e.g. a dimeric Lys-boroPro derivative with an adipate spacer are described.

IT **202203-11-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

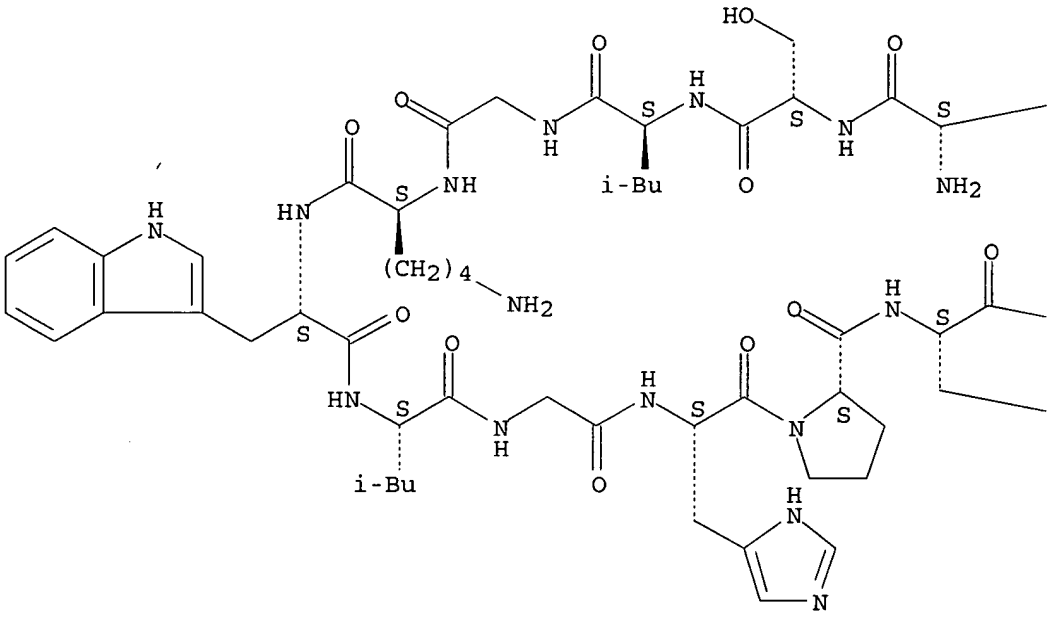
(peptide-based multivalent compds. for crosslinking immune cell receptors, and uses thereof)

RN 202203-11-0 HCAPLUS

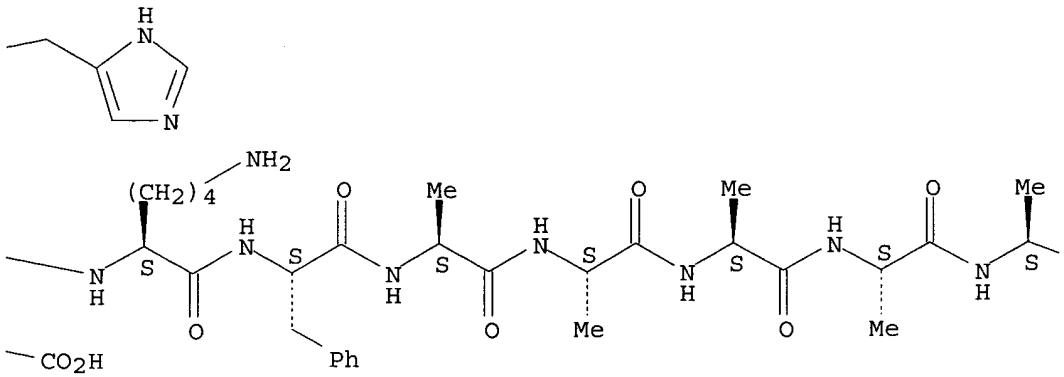
CN L-Alaninamide, L-histidyl-L-seryl-L-leucylglycyl-L-lysyl-L-tryptophyl-L-leucylglycyl-L-histidyl-L-prolyl-L-α-aspartyl-L-lysyl-L-phenylalanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-N-[(5S)-5-amino-6-[(2S)-2-borono-1-pyrrolidinyl]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

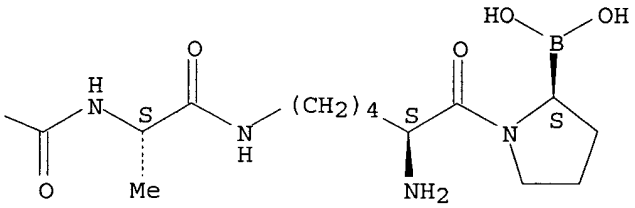
PAGE 1-A



PAGE 1-B



PAGE 1-C



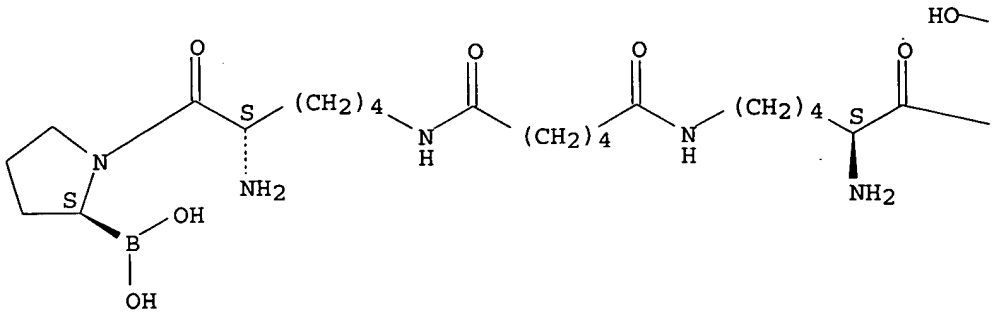
IT **202203-08-5 202203-10-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide-based multivalent compds. for crosslinking immune cell receptors, and uses thereof)

RN 202203-08-5 HCAPLUS

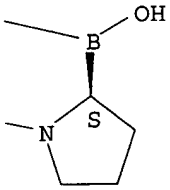
CN Boronic acid, [(1,6-dioxo-1,6-hexanediyl)bis[imino[(2S)-2-amino-1-oxo-6,1-hexanediyl]-(2S)-1,2-pyrrolidinediyl]]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



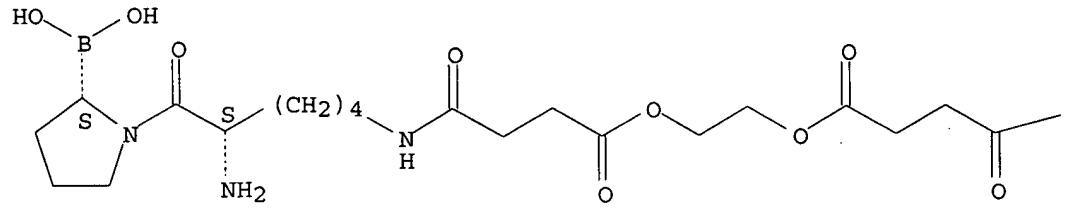
PAGE 1-B



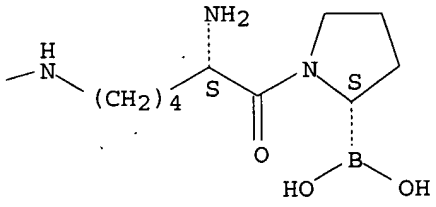
RN 202203-10-9 HCAPLUS
CN Butanoic acid, 4-[[(5S)-5-amino-6-[(2S)-2-borono-1-pyrrolidinyl]-6-oxohexyl]amino]-4-oxo-, 1,1'-(1,2-ethanediyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 184 THERE ARE 184 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:495164 HCAPLUS
DOCUMENT NUMBER: 131:139502
TITLE: Method of regulating glucose metabolism, and reagents related thereto
INVENTOR(S): **Bachovchin, William W.; Plaut, Andrew G.**; Drucker, Daniel J.
PATENT ASSIGNEE(S): Trustees of Tufts University, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938501	A2	19990805	WO 1999-US2294	19990202
WO 9938501	A3	20000113		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319195	AA	19990805	CA 1999-2319195	19990202
AU 9924935	A1	19990816	AU 1999-24935	19990202
AU 766219	B2	20031009		
EP 1052994	A2	20001122	EP 1999-904558	19990202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002501889	T2	20020122	JP 2000-529234	19990202
EP 1520582	A2	20050406	EP 2004-29691	19990202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6803357	B1	20041012	US 2001-601432	20010105
US 2003153509	A1	20030814	US 2002-190267	20020703
US 6890898	B2	20050510		
AU 2003264609	A1	20040108	AU 2003-264609	20031128
US 2004176307	A1	20040909	US 2004-794316	20040304
JP 2005041885	A2	20050217	JP 2004-327376	20041111

PRIORITY APPLN. INFO.:		
US 1998-73409P	P	19980202
EP 1999-904558	A3	19990202
JP 2000-529234	A3	19990202
WO 1999-US2294	W	19990202
US 2000-628225	A1	20000728
US 2002-190267	A1	20020703

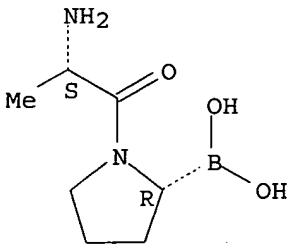
OTHER SOURCE(S): MARPAT 131:139502

AB The present invention provides methods and compns. for modification and regulation of glucose and lipid metabolism, generally to reduce insulin resistance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia (such as chylomicrons, VLDL and LDL), and to regulate body fat and more generally lipid stores, and, more generally, for the improvement of metabolism disorders, especially those associated with diabetes, obesity and/or atherosclerosis.

IT **139649-82-4P 139649-83-5P**
RL: PNU (Preparation, unclassified); PREP (Preparation)

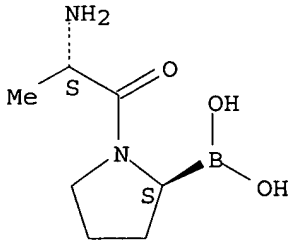
(method of regulating glucose metabolism, and reagents related thereto)
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 139649-83-5 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:233987 HCAPLUS
DOCUMENT NUMBER: 130:264434
TITLE: Stimulation of hematopoietic cells in vitro using inhibitors of dipeptidyl peptidase IV in the absence of cytokines
INVENTOR(S): **Bachovchin, William**; Wallner, Barbara
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916864	A1	19990408	WO 1998-US20343	19980929

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,

	FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA	2304206	AA	19990408	CA 1998-2304206	19980929
AU	9895887	A1	19990423	AU 1998-95887	19980929
AU	743996	B2	20020214		
EP	1019494	A1	20000719	EP 1998-949595	19980929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR	9813233	A	20000822	BR 1998-13233	19980929
TR	200000815	T2	20001221	TR 2000-200000815	19980929
US	6258597	B1	20010710	US 1998-162934	19980929
JP	2001518290	T2	20011016	JP 2000-513935	19980929
NZ	503359	A	20020201	NZ 1998-503359	19980929
IL	135068	A1	20040328	IL 1998-135068	19980929
NO	2000001583	A	20000529	NO 2000-1583	20000327
US	2001018210	A1	20010830	US 2001-812528	20010320
US	6703238	B2	20040309		
AU	778608	B2	20041216	AU 2002-40628	20020513
US	2004152192	A1	20040805	US 2003-725952	20031201
AU	2005201141	A1	20050407	AU 2005-201141	20050316
JP	2006081554	A2	20060330	JP 2005-329518	20051114
PRIORITY APPLN. INFO.:				US 1997-60306P	P 19970929
				AU 1998-95887	A3 19980929
				JP 2000-513935	A3 19980929
				US 1998-162934	A1 19980929
				WO 1998-US20343	W 19980929
				US 2001-812528	A1 20010320
				AU 2002-40628	A 20020513

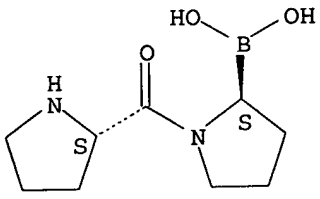
AB The present invention provides methods and compns. for stimulating the growth and differentiation of hematopoietic cells in vitro. Advantageously, the methods of the invention do not require the addition of exogenously added cytokines to support the stimulation of hematopoietic cells in vitro. The methods involve contacting the hematopoietic cells with an inhibitor of dipeptidyl peptidase (DPIV) in the absence of exogenously provided cytokines. Accordingly, the methods and compns. of the invention are useful for increasing the number of hematopoietic cells in vitro and/or causing the differentiation of early progenitor cells. The stimulated hematopoietic cells of the invention are useful for the treatment of disorders that are characterized by a reduced number of hematopoietic cells or their precursors in vivo. Such conditions occur frequently in patients who are immunosuppressed, for example, as a consequence of chemotherapy and/or radiation therapy for cancer.

IT **150035-54-4 174276-10-9 202203-06-3**
202203-06-3D, conjugate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stimulation of hematopoietic cells in vitro using inhibitors of dipeptidyl peptidase IV in the absence of cytokines)

RN 150035-54-4 HCAPLUS

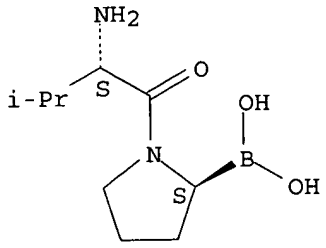
CN Boronic acid, [(2S)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



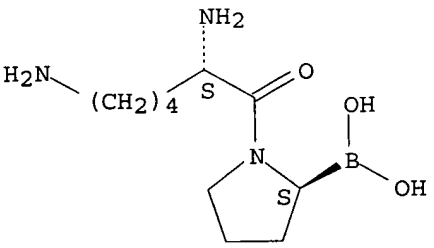
RN 174276-10-9 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



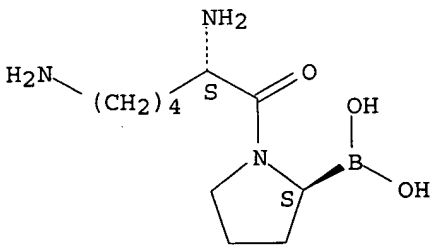
RN 202203-06-3 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 202203-06-3 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:58967 HCAPLUS
DOCUMENT NUMBER: 128:136531
TITLE: Multivalent compounds for crosslinking receptors and therapeutic uses thereof
INVENTOR(S): **Bachovchin, William W.**
PATENT ASSIGNEE(S): Trustees of Tufts College, USA; Bachovchin, William W.
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800439	A2	19980108	WO 1997-US11279	19970627
WO 9800439	A3	20000824		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5965532	A	19991012	US 1997-837305	19970411
AU 9737927	A1	19980121	AU 1997-37927	19970627
AU 739241	B2	20011004		
EP 938498	A1	19990901	EP 1997-934862	19970627
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE				
JP 2000515500	T2	20001121	JP 1998-504344	19970627

PRIORITY APPLN. INFO.:			
	US 1996-671756	A	19960628
	US 1996-77180P	P	19960628
	US 1997-837305	A	19970411
	WO 1997-US11279	W	19970627

AB Synthetic crosslinking homobivalent and heterobivalent compds. have been designed and developed. These compds. are low in mol. weight, have antagonistic or agonistic activity, and induce the association between two identical or similar natural receptors (homobivalent compds.) or induce the association between two different natural receptors (heterobivalent compds.). Thus, Lys-boroPro linked, through the ε-amino groups of Lys, to a second Lys-boroPro mol. by adipic acid (KbP2Ad) or by ethylene glycol bissuccinate (KbP2EGS) were prepared Both KbP2Ad and KbP2EGS stimulated T cell line H9 to produce IL-2. A second type of multivalent compound designed to crosslink CD26 and TCR, i.e., Lys-boroPro linked to myelin proteolipid protein peptide 139-151, strongly enhanced T cell response to the T cell receptor-recognized antigen.

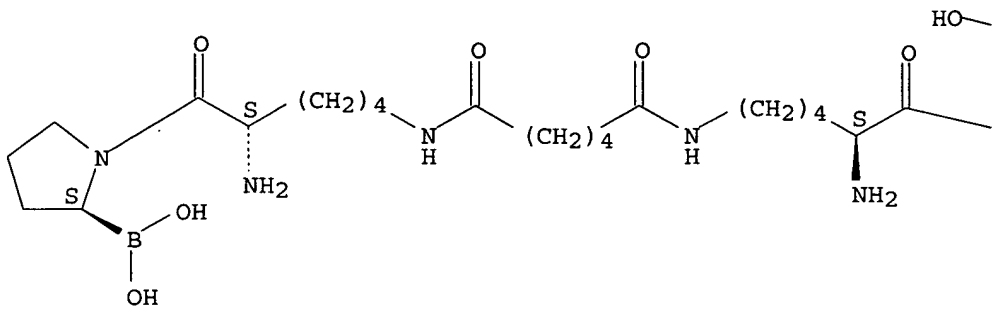
IT **202203-08-5P 202203-10-9P 202203-11-0P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(multivalent compds. for crosslinking receptors and therapeutic uses thereof)

RN 202203-08-5 HCAPLUS
CN Boronic acid, [(1,6-dioxo-1,6-hexanediyl)bis[imino[(2S)-2-amino-1-oxo-6,1-

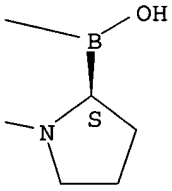
hexanediyl]-(2S)-1,2-pyrrolidinediyl]]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



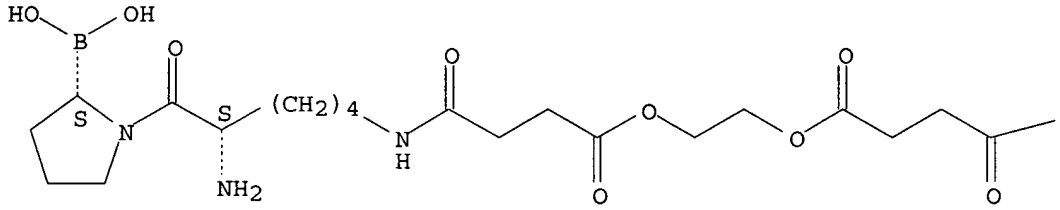
PAGE 1-B



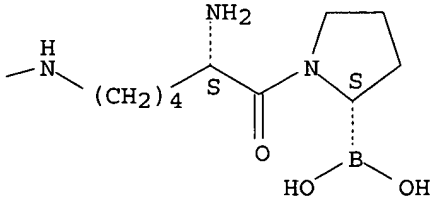
RN 202203-10-9 HCAPLUS
CN Butanoic acid, 4-[[(5S)-5-amino-6-[(2S)-2-borono-1-pyrrolidinyl]-6-oxohexyl]amino]-4-oxo-, 1,1'-(1,2-ethanediyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

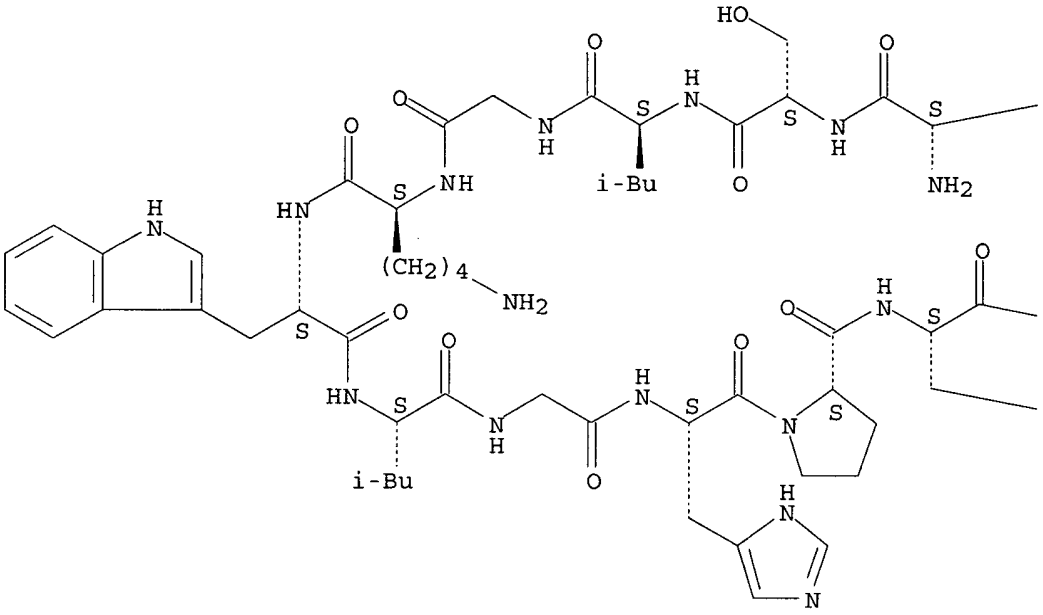


RN 202203-11-0 HCAPLUS

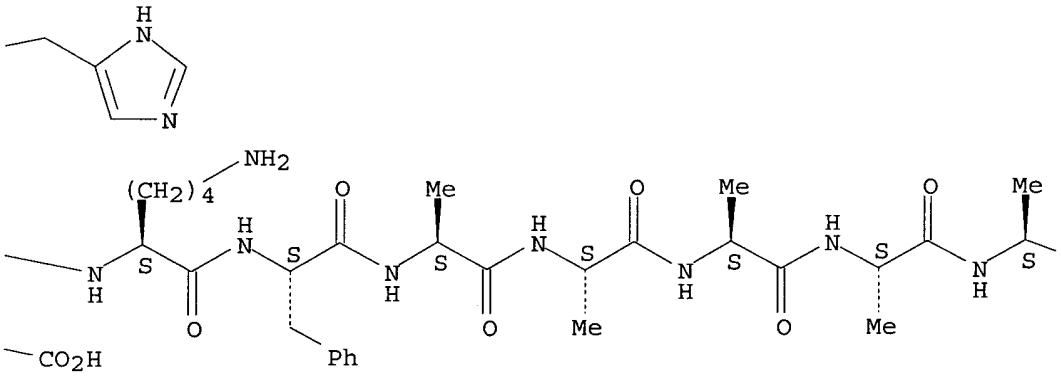
CN L-Alaninamide, L-histidyl-L-seryl-L-leucylglycyl-L-lysyl-L-tryptophyl-L-leucylglycyl-L-histidyl-L-prolyl-L-α-aspartyl-L-lysyl-L-phenylalanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-N-[(5S)-5-amino-6-[(2S)-2-borono-1-pyrrolidinyl]-6-oxohexyl]- (9CI) (CA INDEX NAME)

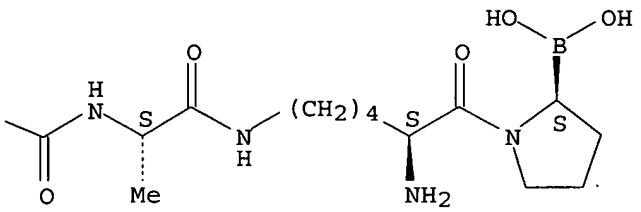
Absolute stereochemistry.

PAGE 1-A



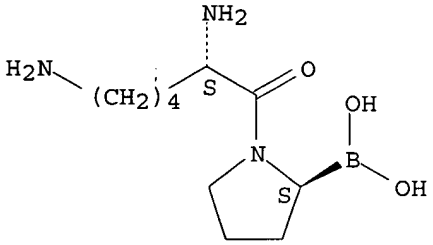
PAGE 1-B





IT **202203-06-3D**, compds. containing
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multivalent compds. for crosslinking receptors and therapeutic uses thereof)
RN 202203-06-3 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



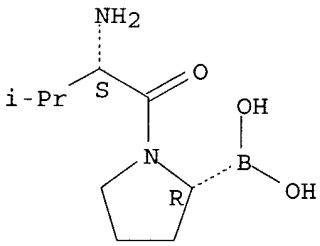
L36 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:26975 HCAPLUS
DOCUMENT NUMBER: 124:203071
TITLE: Solution structures of the DP IV (CD26) inhibitor Val-boroPro determined by NMR spectroscopy
AUTHOR(S): Guenther, Ulrich L.; Sudmeier, James L.; Coutts, Simon J.; Snow, Roger J.; Barton, Randall W.; **Bachovchin, William W.**
CORPORATE SOURCE: Department Biochemistry, Tufts University School Medicine, Boston, MA, 02111, USA
SOURCE: Magnetic Resonance in Chemistry (1995), 33(12), 959-70
CODEN: MRCHEG; ISSN: 0749-1581
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-Val-L-boroPro, a potent DP IV (CD26) inhibitor, and its non-inhibitory diastereomer L-Val-D-boroPro, were studied by 1D 1H and 11B NMR and by 2D 1H NMR methods in aqueous solution Complete 1D 1H NMR fine structures were

computer analyzed to obtain the 1H chemical shifts and spin coupling consts. Dihedral angles were derived from coupling consts. on the basis of the Altona equation (i.e. an improved Karplus equation). The structures and populations of proline ring conformations were determined with the aid of pseudo-rotation anal. Good agreement between the distances derived from NOESY data and dihedral angle-constrained force-field calcns. was obtained. Structural anal. allowed the identification of the absolute stereochem. of the α-carbon of the proline residue, and showed that the active inhibitor is the diastereomer which is homochiral with L-proline. L-Val-L-boroPro exists largely in a single conformer, in contrast to L-VAl-D-boroPro, which adopts two proline conformations in a 2:1 ratio. Anal. of 1H and 11B NMR spectra proves that inactivation of the inhibitor at physiol. pH results from a cyclization reaction in which the free N-terminal nitrogen atom forms a covalent bond with the B atom.

IT **149682-77-9 174276-10-9**
RL: PRP (Properties)
(solution structure of L-Val-L-boroPro and L-Val-D-boroPro determined by NMR spectroscopy)

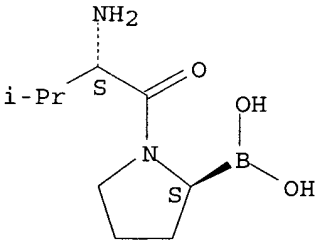
RN 149682-77-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174276-10-9 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:702091 HCAPLUS
DOCUMENT NUMBER: 123:74880
TITLE: Use of inhibitors of dipeptidyl aminopeptidase to block entry of HIV into cells
INVENTOR(S): **Bachovchin, William W.**
PATENT ASSIGNEE(S): Trustees of Tufts College, USA

SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

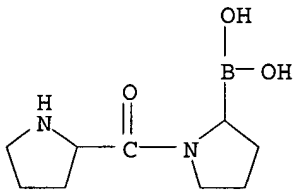
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511689	A1	19950504	WO 1993-US10423	19931029

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

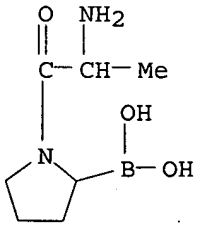
PRIORITY APPLN. INFO.: WO 1993-US10423 19931029
OTHER SOURCE(S): MARPAT 123:74880

AB Dipeptidyl aminopeptidase Type IV (DP IV) inhibitors X-Pro-Y-Boropro [X, Y = any amino acid (including proline)] are provided for blocking entry of HIV into uninfected CD26+ cells by blocking CD26. Pro-boroPro has a Ki for DP IV of approx. 1 x 10-8 M, and it decomps. in aqueous solution at room temperature (20-25°) with a half-life of approx. 1.5 h. Although the affinity of Pro-boroPro is approx. 10-fold less than that of Ala-boroPro (preparation described), the increased stability of the former is advantageous.

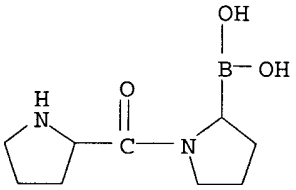
IT **133745-65-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dipeptidyl aminopeptidase inhibitors, and their preparation, to block HIV entry into cell)
RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



IT **127292-29-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dipeptidyl aminopeptidase inhibitors, and their preparation, to block HIV entry into cell)
RN 127292-29-9 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



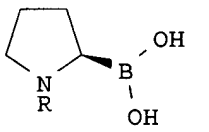
L36 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:637571 HCAPLUS
DOCUMENT NUMBER: 123:81509
TITLE: Inhibition of CD26 enzyme activity with Pro-boropro stimulates rat granulocyte/macrophage colony formation and thymocyte proliferation in vitro
AUTHOR(S): Bristol, Lynn A.; **Bachovchin, William**; Takacs, Laszlo
CORPORATE SOURCE: Natl. Inst. Alcohol Alcohol Abuse, Natl. Inst. Health, Rockville, MD, USA
SOURCE: Blood (1995), 85(12), 3602-9
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD26 dipeptidyl peptidase (DPPIV) is involved in the regulation of proliferation of some hematopoietic and T-lineage cells. Here, we show that Pro-boropro a potent inhibitor of DPP activity has a costimulating effect in hematopoietic colony assays for macrophage and, to a lesser extent, for granulocyte colonies and has a stimulating effect in organ cultures of immature thymocytes. Based on these and other evidences, we propose that the mechanism by which CD26 regulates proliferation is associated with its DPP activity.
IT **133745-65-0**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of CD26 dipeptidyl peptidase activity with pro-boropro stimulates rat granulocyte/macrophage colony formation and thymocyte proliferation in vitro)
RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



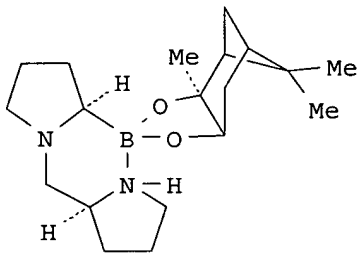
L36 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:391825 HCAPLUS
DOCUMENT NUMBER: 122:181492
TITLE: IgA-specific prolyl endopeptidases: Serine type
AUTHOR(S): **Plaut, Andrew G.; Bachovchin, William W.**
CORPORATE SOURCE: School Medicine, Tufts University, Boston, MA, 02111, USA
SOURCE: Methods in Enzymology (1994), 244(Proteolytic Enzymes: Serine and Cysteine Peptidases), 137-51
CODEN: MENZAU; ISSN: 0076-6879
DOCUMENT TYPE: Journal
LANGUAGE: English

AB After a discussion of bacteria producing IgA proteases, synthesis and secretion of serine-type IgA proteinases, and their specificity, the assay of IgA proteinases was detailed. The purification, storage, structure, catalytic mechanism, synthetic peptide inhibitors, and antibody inhibition of IgA proteinases were then discussed. Finally, the epidemiol. investigation of IgA proteinases and the role of IgA proteinases in infectious processes were mentioned.

L36 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:183432 HCAPLUS
DOCUMENT NUMBER: 122:240402
TITLE: Studies on Proline Boronic Acid Dipeptide Inhibitors of Dipeptidyl Peptidase IV: Identification of a Cyclic Species Containing a B-N Bond
AUTHOR(S): Snow, Roger J.; **Bachovchin, William W.**; Barton, Randall W.; Campbell, Scot J.; Coutts, Simon J.; Freeman, Dorothy M.; Gutheil, William G.; Kelly, Terence A.; Kennedy, Charles A.; et al.
CORPORATE SOURCE: Department of Medicinal Chemistry Pharmacology, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 06877, USA
SOURCE: Journal of the American Chemical Society (1994), 116(24), 10860-9
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB The proline boronic acid dipeptides I (R = H-Ala, H-Pro, H-Val) are very potent inhibitors of the enzyme dipeptidyl peptidase IV (DPP IV or CD26), found on the surface of T-cells, and are a new class of immunosuppressants. The efficient synthesis of the free boronic acids as single enantiomers is described, and the absolute configuration determined I lose DPP IV inhibitory activity in solution: this is shown to be due to the reversible formation of a cyclic species analogous to a diketopiperazine, containing a B-N bond. The cyclic compds., both as the free boronic acids and as the pinanediol esters, were isolated and characterized by 1H and 11B NMR, and in the case of II, by x-ray crystallog. The cyclization is pH dependent, with the open form favored at low pH, while the cyclic form predominates at neutral pH. Both the rate and extent of cyclization depend on the N-terminal amino acid. The rates of cyclization have been measured by 1H NMR and shown to correlate with the decrease in DPP IV inhibitory activity. I (R = H-Val) cyclizes more slowly, and to a lesser extent than I (R = H-Ala, H-Pro), which is predicted to lead to greater immunosuppressive potency in vivo.
IT **150080-09-4P 162185-16-2P 162185-17-3P**

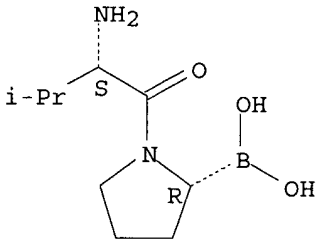
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, cyclization, and dipeptidyl peptidase IV inhibitory activity of proline boronic acid dipeptides)

RN 150080-09-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

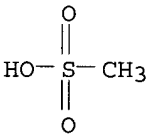
CRN 149682-77-9
CMF C9 H19 B N2 O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

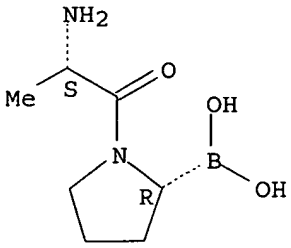


RN 162185-16-2 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, [R-(R*,S*)]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

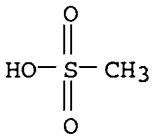
CRN 139649-82-4
CMF C7 H15 B N2 O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

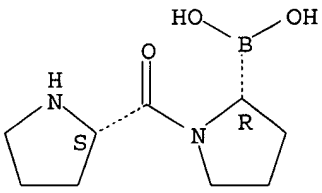


RN 162185-17-3 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]-, [R-(R*,S*)]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

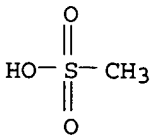
CRN 150572-30-8
CMF C9 H17 B N2 O3

Absolute stereochemistry.



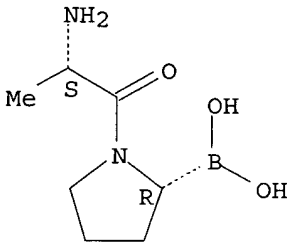
CM 2

CRN 75-75-2
CMF C H4 O3 S



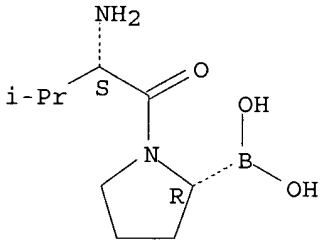
IT **139649-82-4P 149682-77-9P 150572-30-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, cyclization, and dipeptidyl peptidase IV inhibitory activity of proline boronic acid dipeptides)
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



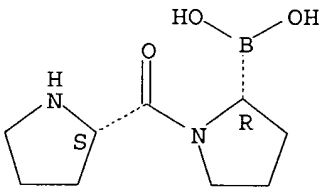
RN 149682-77-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150572-30-8 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:64843 HCAPLUS
DOCUMENT NUMBER: 122:26520
TITLE: Solution Structures of Active and Inactive Forms of the DP IV (CD26) Inhibitor Pro-boroPro Determined by

NMR Spectroscopy

AUTHOR(S): Sudmeier, James L.; Gunther, Ulrich L.; Gutheil, William G.; Coutts, Simon J.; Snow, Roger J.; Barton, Randall W.; **Bachovchin, William W.**

CORPORATE SOURCE: School of Medicine, Tufts University, Boston, MA, 02111, USA

SOURCE: Biochemistry (1994), 33(41), 12427-38
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

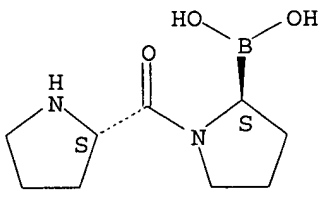
LANGUAGE: English

AB Synthesis of the boronic acid analog of the dipeptide Pro-Pro yields a mixture of diastereomers Pro-L-boroPro and Pro-D-boroPro, one of which is a potent inhibitor [Ki = 16 pM; Gutheil, W. G., & Bachovchin, W. W. (1993) Biochem. 32, 8723-8731] of dipeptidyl amino peptidase type IV (DP IV), also known as CD26. The structures of both diastereomers are determined here in aqueous solution by 1D and 2D NMR of 1H, 13C, and11B, and force-field calcns., and the inhibitor is proven to have the L-L configuration. At low pH values (.apprx.2), both diastereomers are trans with respect to the peptide bond. Populations of proline ring conformers are determined by pseudorotation anal., using vicinal proton spin-coupling consts. obtained by computer anal. of 1D 1H NMR spectral fine structure. At neutral pH values, the Pro-boroPro inhibitor of DP IV undergoes slow, reversible inactivation (Gutheil & Bachovchin, 1993). By structural determination of the decomposition products of both diastereomers, the process is shown here to involve formation of a six-membered ring between the residues by trans-cis conversion and formation of a B-N bond, producing chiral nitrogen atoms in both cases having the S configuration. Analogy to cyclic dipeptides suggests the new compds. be named cyclo(Pro-L-boroPro) and cyclo(Pro-D-boroPro).

IT **150035-54-4 150572-30-8**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(solution structures of active and inactive forms of dipeptidyl amino peptidase IV (CD26) inhibitor pro-boroPro determined by NMR spectroscopy)

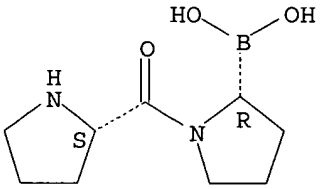
RN 150035-54-4 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150572-30-8 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

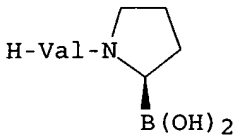


L36 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:506375 HCAPLUS
DOCUMENT NUMBER: 121:106375
TITLE: Human immunodeficiency virus 1 Tat binds to dipeptidyl aminopeptidase IV (CD26): a possible mechanism for Tat's immunosuppressive activity
AUTHOR(S): Gutheil, William G.; Subramanyam, Meena; **Flentke, George R.**; Sanford, David G.; Munoz, Eduardo; Huber, Brigitte T.; **Bachovchin, William W.**
CORPORATE SOURCE: Deps. Biochemistry and Pathology, Sch. Med., Boston, MA, 02111, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(14), 6594-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

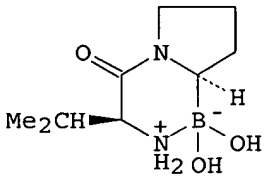
AB The human immunodeficiency virus 1 (HIV-1) Tat protein suppresses antigen-induced, but not mitogen-induced, activation of human T cells when added to T-cell cultures. This activity is potentially pertinent to the development of AIDS because lymphocytes from HIV-infected individuals exhibit a similar antigen-specific dysfunction. Here the authors report that Tat binds with high affinity to the T-cell activation mol. dipeptidyl aminopeptidase IV (DP IV), also known as CD26. This mol. occurs on the surface of CD4+ cells responsible for the recall antigen response and appears to play an essential role in this response. Tat binds to both the cell surface and soluble forms of DP IV at physiol. salt concns. without inhibiting the protease activity of DP IV against small chromogenic substrates used to assay activity, but Tat markedly inhibits the activity of DP IV at lower salt concns. The kinetics of inhibition indicate the affinity of Tat for DP IV varies from 20 pM to 11 nM, and the activity of the Tat-DP IV complex varies from 13-100%, as the NaCl concentration varies from 0-140 mM. Cytofluorometry expts. demonstrate that Tat competes with anti-Ta1, a monoclonal antibody (mAb) specific for DP IV, for binding to cell surface DP IV, thus indicating that Tat binds DP IV at or near the Ta1 epitope. Moreover, the anti-Ta1 mAb blocks the immunosuppressive activity of Tat. The high affinity of Tat for DP IV, previous evidence implicating DP IV in antigen-specific T-cell activation events, and the ability of anti-Ta1 mAb to block the immunosuppressive effect of Tat make DP IV a plausible receptor for Tat's immunosuppressive activity.

L36 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:218507 HCAPLUS
DOCUMENT NUMBER: 120:218507
TITLE: Immunosuppressive boronic acid dipeptides: correlation between conformation and activity
AUTHOR(S): Kelly, Terence A.; Adams, Julian; **Bachovchin, William W.**; Barton, Randall W.; Campbell, Scot J.; Coutts, Simon J.; Kennedy, Charles A.; Snow, Roger

J.
CORPORATE SOURCE: Dep. Med. Chem., Boehringer Ingelheim Pharm. Inc., Ridgefield, CT, 06877, USA
SOURCE: Journal of the American Chemical Society (1993), 115(26), 12637-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

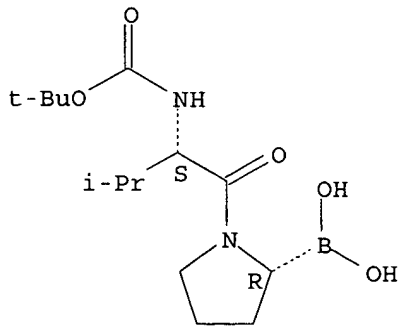


II

AB The correlation between the conformation and the immunosuppressive activity of the boronic acid-containing dipeptide I was demonstrated. The rate of cyclization of I to II was measured by 1H-NMR techniques while the corresponding time-dependent loss of ability of the material to inhibit dipeptidyl peptidase IV was characterized via an enzyme assay. The rate consts. thus obtained point to II as being responsible for the deactivation of this inhibitor. Furthermore the reversibility of the cyclization was effected and showed to restore inhibitory activity against the enzyme. The enzymic consequences of the ensuring equilibrium between active and inactive conformations is discussed.

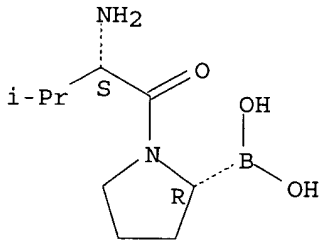
IT **149682-78-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in preparation of boronic acid dipeptide)
RN 149682-78-0 HCAPLUS
CN Carbamic acid, [1-[(2-borono-1-pyrrolidinyl)carbonyl]-2-methylpropyl]-, C-(1,1-dimethylethyl) ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



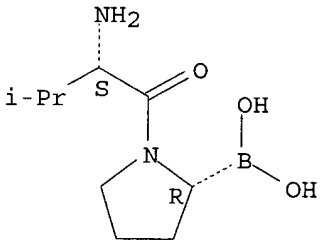
IT **149682-77-9P 153737-95-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, cyclization, and enzyme inhibitory activity of)
RN 149682-77-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153737-95-2 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

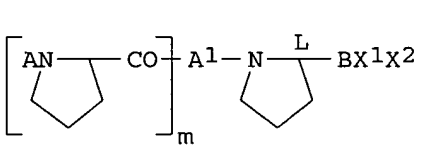
L36 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:603868 HCAPLUS
DOCUMENT NUMBER: 119:203868
TITLE: Preparation of peptidylboronate derivatives as inhibitors of dipeptidyl-aminopeptidase type IV
INVENTOR(S): **Bachovchin, William W.; Plaut, Andrew G.; Flentke, George R.**
PATENT ASSIGNEE(S): New England Medical Center Hospitals, Inc., USA; Tufts University
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9308259	A2	19930429	WO 1992-US9026	19921021
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
EP 610317	A1	19940817	EP 1992-922300	19921021
EP 610317	B1	20010131		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, SE				

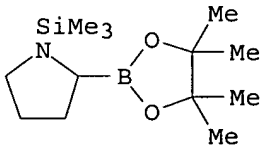
JP 07504158	T2	19950511	JP 1992-507912	19921021
EP 1050540	A2	20001108	EP 2000-201402	19921021
EP 1050540	A3	20020102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE				
AT 199016	E	20010215	AT 1992-922300	19921021
ES 2153831	T3	20010316	ES 1992-922300	19921021
CA 2121369	C	20030429	CA 1992-2121369	19921021
US 5462928	A	19951031	US 1993-93302	19930715
US 6825169	B1	20041130	US 1997-950542	19971015
HK 1015611	A1	20011214	HK 1998-115813	19981228
GR 3035730	T3	20010731	GR 2001-400582	20010406
US 2004229820	A1	20041118	US 2004-775598	20040210
PRIORITY APPLN. INFO.:			US 1991-781552	A 19911022
			US 1990-510274	B2 19900414
			EP 1992-922300	A3 19921021
			WO 1992-US9026	W 19921021
			US 1993-93302	A3 19930715
			US 1995-459654	B1 19950602
			US 1997-950542	A1 19971015

OTHER SOURCE(S): MARPAT 119:203868

GI



I



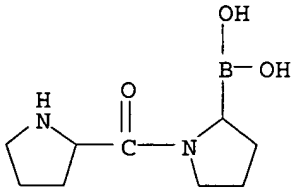
II

AB Title compds. I; m = 0-10; (A,A1 = L-amino acid residues; X1,X2 = OH, group capable of being hydrolyzed to a hydroxyl group at physiol. pH), were prepared Thus, allyl bromide was hydroborated with catecholborane at 100° to give 49% 3-bromopropylboronate catechol ester which was transesterified with pinacol followed by homologation with CH2Cl2/BuLi to give 4-bromo-1-chlorobutylboronate pinacol ester. This was added to a mixture of hexamethyldisilazane and BuLi in THF at -78°-room temperature followed by distillation to give boroproline (boroPro) derivative II. This was desilylated with HCl/dioxane and coupled with BOC-Ala-OH using isobutyl chloroformate/N-methylmorpholine followed by deprotection to give H-Ala-boroPro, which inhibited dipeptidyl aminopeptidase IV with Ki = 2 nM, and suppressed HIV in A3.5 cells to below detectable levels.

IT **133745-65-0P 139649-82-4P 150035-54-4P 150572-30-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as inhibitor of dipeptidyl aminopeptidase IV)

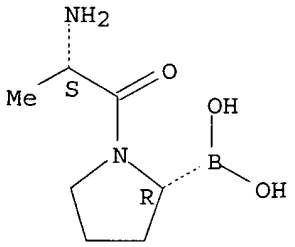
RN 133745-65-0 HCAPLUS

CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



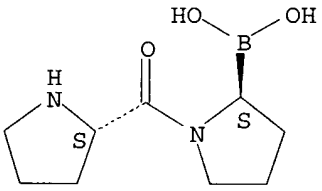
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



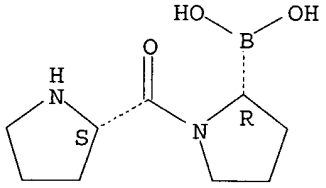
RN 150035-54-4 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

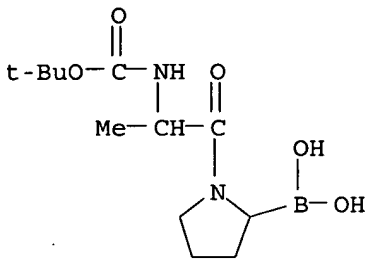


RN 150572-30-8 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **127292-30-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for dipeptidylboronate derivative dipeptidyl
aminopeptidase IV inhibitor)
RN 127292-30-2 HCAPLUS
CN Carbamic acid, [2-(2-borono-1-pyrrolidinyl)-1-methyl-2-oxoethyl]-, C-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

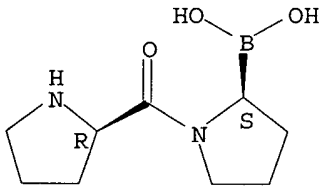


L36 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:554644 HCAPLUS
DOCUMENT NUMBER: 119:154644
TITLE: Separation of L-proline-DL-boronylproline into its component diastereomers and kinetic analysis of their inhibition of dipeptidyl peptidase IV. A new method for the analysis of slow, tight binding inhibition
AUTHOR(S): Gutheil, William G.; **Bachovchin, William W.**
CORPORATE SOURCE: Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SOURCE: Biochemistry (1993), 32(34), 8723-31
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The potent dipeptidyl peptidase IV (DP IV) inhibitor, L-proline-DL-boronylproline (L-Pro-DL-boroPro) was fractionated into its component L-L and L-D diastereomers by C18 HPLC, and the binding of the purified diastereomers to pig kidney DP IV was analyzed. Inhibition kinetics confirmed that the L-L diastereomer was a potent inhibitor of DP IV, with a Ki of 16 pM. The L-D isomer bound at least 1000-fold more weakly than the L-L isomer, if it bound at all, as the .apprx.200-fold weaker inhibition observed for the purified L-D isomer was shown here to be due entirely to the presence of a small amount (0.59%) of the L-L diastereomer contaminating the L-D preparation The instability of Pro-boroPro, together with its very high affinity for DP IV and the time dependence of the inhibition, made a rigorous kinetic anal. of its binding to DP IV difficult. Here, a method was developed which took advantage of the slow rate at which the inhibitor dissocs. from the enzyme. The method involved preincubating DP IV and the inhibitor without substrate and then assaying the free enzyme by the addition of substrate and following its hydrolysis for a period of time which is short relative to the dissociation rate of the inhibitor. Data from expts. in which the preincubation time was sufficient for enzyme and inhibitor to reach equilibrium were analyzed by fitting to an appropriate form of the quadratic equation and yielded a Ki of 16 pM. Data from expts. in which the incubation time was insufficient to establish equilibrium, i.e., within the slow-binding regime, were analyzed by fitting to an integrated rate equation. The appropriate integrated rate equation for an A + B .dblarw. C system going to equilibrium does not appear to have been previously derived. The anal. of the slow-binding curves yielded a Ki of 16 pM, in agreement with that of 16 pM determined in the equilibrium titrns., and a bimol. rate constant of association, kon, of 5.0 x 106 M-1 s-1. The exptl. determined kon and Ki values indicated that the dissociation rate constant, koff, was 78 x 10-6 s-1 (t1/2 = 150 min). The slow-binding curves were shown here to fit a simple E + I .dblarw. EI model, indicating that it is not necessary to invoke a 2-step mechanism to explain the inhibition kinetics.

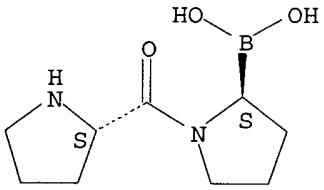
IT **150035-53-3**
RL: BIOL (Biological study)
(dipeptidyl peptidase IV of kidney inhibition by, kinetics and mechanism of)
RN 150035-53-3 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

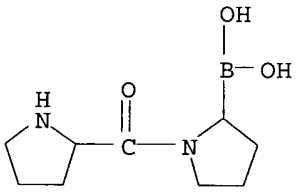


IT **150035-54-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dipeptidyl peptidase IV of kidney response to)
RN 150035-54-4 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-pyrrolidinylcarbonyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **133745-65-0**
RL: PROC (Process)
(resolution of)
RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

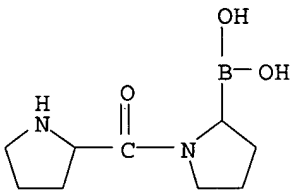


L36 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:486040 HCAPLUS
DOCUMENT NUMBER: 119:86040
TITLE: Producing increased numbers of hematopoietic cells by

administering inhibitors of dipeptidyl peptidase IV
INVENTOR(S): Takaco, Laszlo; Bristol, Lynn A.; **Bachovchin, William W.**
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U. S. Pat. Appl., 14 pp. Avail. NTIS Order No. PAT-APPL-7-923,337.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 923337	A0	19930401	US 1992-923337		19920731
WO 9403055	A1	19940217	WO 1993-US7173		19930730
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9347943	A1	19940303	AU 1993-47943		19930730
PRIORITY APPLN. INFO.:			US 1992-923337	A	19920731
			WO 1993-US7173	W	19930730

AB An inhibitor of dipeptidyl peptidase IV is administered to patients for producing increased number of hematopoietic cells. As an example, human subjects suffering from a deficiency of hematopoietic cells (e.g. AIDS patients) were treated i.v. with the inhibitor of 1-10 mg/μg.
IT **133745-65-0**
RL: BIOL (Biological study)
(dipeptidyl peptidase IV inhibitor, as hematopoiesis promoter)
RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

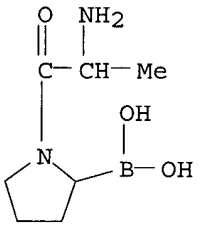


L36 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:5549 HCAPLUS
DOCUMENT NUMBER: 118:5549
TITLE: Involvement of dipeptidyl peptidase IV in an in vivo immune response
AUTHOR(S): Kubota, T.; **Flentke, G. R.**; **Bachovchin, W. W.**; Stollar, B. D.
CORPORATE SOURCE: Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SOURCE: Clinical and Experimental Immunology (1992), 89(2), 192-7
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dipeptidyl peptidase IV (DP IV) is a serine protease that selectively cleaves X-Pro dipeptides from polypeptides and proteins. Among blood cells, this enzyme occurs preferentially on the surface of CD4+ T cells and the amount of enzyme activity increases with T cell activation. In

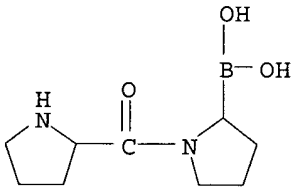
previous work, two potent and specific peptidyl-boronic acid inhibitors of DP IV, Ala-boroPro and Pro-boroPro, were synthesized and Pro-boroPro was shown to suppress antigen-specific proliferative responses of T cells in vitro. This study tested the in vivo effects of these inhibitors. The injection (s.c.) of Ala-boroPro or Pro-boroPro into BALB/c mice inhibited DP IV activity in serum and spleen cell suspensions. Repeated injections of more than 10 μg of Ala-boroPro or Pro-boroPro at 12 h intervals maintained in vivo DP IV activity at less than 30% of the normal level. Repeated injections of the inhibitors during the primary, secondary or tertiary immune response to bovine serum albumin (BSA) reduced anti-BSA antibody production Without inhibitor, immunization with BSA was followed by a temporary decrease in serum DP IV activity and then by enhanced serum enzyme activity after several days. These results provide the first direct evidence that DP IV plays an important role in immune responses in vivo.

IT **127292-29-9 133745-65-0**
RL: BIOL (Biological study)
(dipeptidyl peptidase IV of serum and lymphocytes inhibition by, immunity in relation to)

RN 127292-29-9 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



RN 133745-65-0 HCAPLUS
CN Boronic acid, [1-(2-pyrrolidinylcarbonyl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

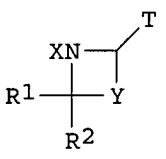


L36 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:633676 HCAPLUS
DOCUMENT NUMBER: 111:233676
TITLE: Preparation of prolylboronate-containing and related peptides as bacterial protease inhibitors
INVENTOR(S): **Bachovchin, William W.**; **Plaut, Andrew G.**; Kettner, Charles A.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

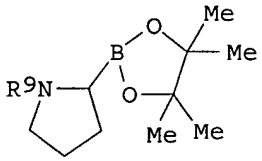
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8903223	A1	19890420	WO 1988-US3506		19881006
W: AU, DK, FI, JP, NO					
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
US 4935493	A	19900619	US 1987-105768		19871006
AU 8928012	A1	19890502	AU 1989-28012		19881006
DK 8906584	A	19891222	DK 1989-6584		19891222
NO 9000081	A	19900108	NO 1990-81		19900108
FI 9000101	A	19900109	FI 1990-101		19900109
PRIORITY APPLN. INFO.:			US 1987-105768	A	19871006
			WO 1988-US3506	A	19881006

OTHER SOURCE(S): CASREACT 111:233676; MARPAT 111:233676
GI



I



II

AB The title compds. [I; R1-R8 = group which does not interfere with site-specific recognition of I by the catalytic site of a post-prolyl-cleaving enzyme; T = BD1D2; D1, D2 = OH, group hydrolyzable to OH at physiol. pH, GCF2CO, P(O)(J)OJ; G = H, F, C1-20 alkyl containing optional N, S, and O atoms; J = alkyl, alkoxy, alkylamino; X = amino acid residue; Y = CR3R4, R3R4CCR5R6, R3R4CCR5R6CR7R8; T is able to form a complex with the catalytic site of a post-prolyl-cleaving enzyme], useful as bacterial protease inhibitors (no data), were prepared Boroproline pinacol derivative II (R9 = H), prepared from allyl bromide and catechol borane, was coupled with BOC-Ala-Pro-OH (BOC = Me3CO2C) using N-methylmorpholine and iso-Bu chloroformate to give after deprotection II (R9 = H-Ala-Pro).

=>